

COMPARITIVE STUDY OF EPIDURAL 0.75%
ROPIVACAINE WITH DEXMEDITOMIDINE AND
0.75% ROPIVACAINE ALONE FOR LOWER LIMB
SURGERIES

DISSERTATION SUBMITTED FOR
DOCTOR OF MEDICINE
BRANCH X (ANAESTHESIOLOGY)
APRIL 2017



THE TAMIL NADU DR.M.G.R MEDICAL UNIVERSITY
CHENNAI, TAMIL NADU

CERTIFICATE FROM DIRECTOR & HOD

This is to certify that this dissertation entitled "**COMPARITIVE STUDY OF EPIDURAL 0.75% ROPIVACAINE WITH DEXMEDITOMIDINE AND 0.75% ROPIVACAINE ALONE FOR LOWER LIMB SURGERIES**"

Submitted by Dr. G HEMA ALAMELU to the FACULTY OF ANAESTHESIOLOGY, THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY, CHENNAI, In partial fulfillment of the requirement in the award of the degree of M.D. degree branch X (ANAESTHESIOLOGY) for the April 2017 examination is a bonafide research work carried out by her under my direct supervision and guidance.

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This is to certify that this dissertation entitled "**COMPARITIVE STUDY OF EPIDURAL 0.75% ROPIVACAINE WITH DEXMEDITOMIDINE AND 0.75% ROPIVACAINE ALONE FOR LOWER LIMB SURGERIES**" is a bonafide record work done by **Dr. G HEMA ALAMELU** under my direct supervision and guidance, submitted to THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY, CHENNAI, In partial fulfillment of University regulation for M.D., branch X Aaesthesiology examination to be held in April 2017.

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DECLARATION

I, DR. G. HEMA ALAMELU declare that the dissertation titled "COMPARITIVE STUDY OF EPIDURAL 0.75% ROPIVACAINE WITH DEXMEDITOMIDINE AND 0.75% ROPIVACAINE ALONE FOR LOWER LIMB SURGERIES" has been prepared by me. This is submitted to the THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY, CHENNAI, In partial fulfillment of the requirement for the award of M.D., degree branch X Aaaesthesiology degree examination to be held in April 2017. I also declare that this dissertation, in part or full was not submitted by me or any other to any other university or board, either in India or abroad for any award, degree or diploma.

Place: Madurai

Date:

Dr. G. HEMA ALAMELU

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LIST OF ABBREVIATIONS

ASA	→	American Society of Anaesthesiologists
DBP	→	Diastolic Blood Pressure
ECG	→	Electrocardiogram
HR	→	Heart rate
Hrs	→	Hours
IV	→	Intravenous
Kg	→	Kilograms
MAP	→	Mean Arterial Pressure
mcg(i)	→	Microgram
ml	→	Milliliter
Mg	→	Milligrams
Min	→	Minutes
mmHg	→	Millimeter of Mercury
SBP	→	Systolic Blood pressure
%	→	Percentage

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INTRODUCTION

Intrathecal anaesthesia and epidural anaesthesia are the popular regional anaesthesia techniques used for lower limb surgeries. Epidural anaesthesia provides effective surgical anaesthesia and extended duration of surgical needs, provides prolonged post operative analgesia, reduces the incidence of hemodynamic changes. Ropivacaine is a relatively new amide local anesthetic. Cardiovascular toxic effects of ropivacaine is minimal compared to bupivacaine. But ropivacaine produces less intense motor blockade.

Strange surroundings of the operation theatre, fear of surgery, the sight and sound of equipments and the masked faces of strange personele makes the patient panic to any extent.

Sedation, stable haemodynamics and prolonged post-operative analgesia are the main desirable qualities of an adjuvant in central neuraxial anaesthesia

Dexmedetomidine is a highly selective α_2 agonist with geater affinity [eight times greater] than clonidine. Dexmedetomidine prolongs the duration of analgesia, motor block and post operative analgesia makes it a very useful adjuvant agent. Hence we compared 0.75% ropivacaine with dexmedetomidine and 0.75% ropivacaine alone.

AIM OF STUDY

The aim of this randomized, prospective study is to compare the synergistic effect of adding dexmedetomidine to 0.75% ropivacaine in epidural anaesthesia for lower limb surgeries regarding

1. Onset and duration of sensory blockade
2. Onset and duration of motor blockade
3. Haemodynamic changes
4. Maximum dermatomal level of analgesia
5. Intensity of motor blockade
6. Sedation
7. Any adverse effects

HISTORICAL BACKGROUND

Sigmund Freud (1856-1939), noticed cocaine's ability to produce numbness of the tongue and provided a small sample to his junior colleague, Carl Koller (1858-1944), an intern who was interested in producing local anaesthesia for operations on the eye. In 1884 Carl Koller used cocaine as topical application over the cornea and conjunctiva to produce anaesthesia for eye surgeries.

Within months of publication of Koller's paper, cocaine started being injected to produce regional anaesthesia and not just topical anaesthesia. In 1885, Halsted used cocaine to block the brachial plexus, and J Leonard Corning, a neurologist, injected cocaine intervertebrally in dogs and in humans to produce pain relief and not to provide operative anaesthesia. Spinal anaesthesia with cocaine was initially produced inadvertently by J Leonard Corning, in 1885 and first used deliberately by August Bier in 1898. On August 15 1898, August Bier and his assistant August Hildebrandt used the Quinckes method of entering the Intrathecal space and injected between 5 and 15 mg of cocaine to produce spinal anaesthesia in six cases for operations on the lower part of the body. They also reported the result of spinal anaesthesia given to each other.

Jean Enthuse Sicard and Fernand Cathelin independently introduced cocaine through the sacral hiatus in 1901, becoming the first practitioners of caudal epidural anaesthesia. 19 years later, a Spanish military surgeon Archile Mario Dogliotti conducted abdominal surgery with single shot lumbar epidural anaesthesia. He identified the epidural space by the sudden loss of resistance noted after the needle had crossed the ligamentum flavum. Manuel Martinez Curbelo, Cuba anaesthesiologist visited to Mayo Clinic in 1947, he watched Tuohy performing continuous spinal anaesthesia. Curbelo performing continuous segmental lumbar epidural anaesthesia with Tuohy needle and silk urethral catheter. Several modifications of the Tuohy-Huber epidural needle have been developed in the more recent past and are being utilized in modern anaesthesia practice.

The toxicity of cocaine, coupled with its vast potential for usefulness in surgery, led to an intensive search for less toxic substitutes. Procaine was synthesized by Einhorn in 1904, but the limitation was its short duration of action. McIsches synthesized Dibucaine in 1925, Uhlmann introduced it clinically. In 1928, Eisleb synthesized Tetracaine and introduced into clinical practice.

Most of the chemical compounds synthesized during this first pharmaceutical period were amino ester derivatives. Most of these amino ester agents were relatively unstable and could not be subjected to repeated autoclaving for sterilization.

In addition, the hydrolysis of aminoesters by enzyme pseudocholinesterase resulted in the formation of para amino benzoic acid which was responsible for reported allergic reactions.

Lidocaine, synthesized in 1943 by Lofgren and Lundquist was a stable compound that was not influenced by repeated exposures to high temperature and thus could be resterilised often. In addition, the metabolites of lidocaine did not include p-amino benzoic acid. Thus allergic reactions were avoided.

Subsequent to lidocaine release, a number of amino amide compounds were synthesized and four eventually found their way into clinical practice. In 1956, Ekenstam in Sweden synthesized Mepivacaine, whose anesthetic properties were similar to lidocaine. In 1959, Lofgren and co workers synthesized prilocaine. Lidocaine and mepivacaine were tertiary amides compounds while prilocaine was secondary amide.

Bupivacaine was produced by Ekenstam in 1956 and introduced into clinical practice in 1963 by Telivuo.

In 1971 Takman synthesized Etidocaine and it was found that etidocaine produced more intense and prolonged motor blockade than sensory blockade, hence not producing ideal perioperative anaesthesia.

Since then bupivacaine is extensively used and became very popular for epidural anaesthesia as well as analgesia, because of its long duration of action and preferential sensory block in lower concentrations. Only drawback of bupivacaine was cardiotoxicity, which when accidentally injected intravascularly. Hence there was a need for introduction of drugs with all the advantages of bupivacaine without the cardiotoxicity.

Ropivacaine identified as a local anaesthetic in 1957, but its testing did not begin until 1988. Ropivacaine was introduced into clinical practice in 1990.

APPLIED ANATOMY

The provide an effective and safe administration of an epidural anaesthesia, anaesthesiologist must familiar with the anatomy of the vertebral column, ligaments and blood supply, the epidural space, spinal canal and associated structures.

The vertebral column contains 33 vertebrae of which 7 cervical, 12 thoracic and 5 lumbar vertebrae, the 5 sacral vertebrae are fused to form the sacrum, and the 4 coccygeal vertebrae are fused to form the coccyx.

The normal spinal column is not a straight one, there are two ventrally convex curvatures in the cervical and lumbar regions, provides a double C appearance for the spinal column.

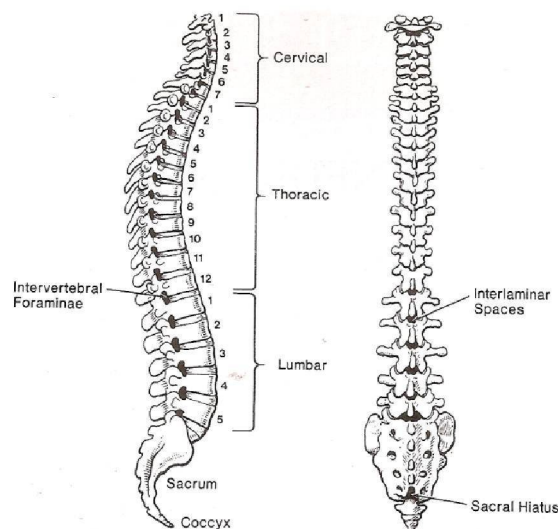


Figure 1: Vertebral column, in lateral view (left) and posterior view (right), illustrating curvatures, lumbar interlaminar spaces and sacral hiatus

Structure of the vertebrae

vertebra is consist of a vertebral body and a bony arch.

Body: It is the bony mass through which the weight of the subject is transmitted.

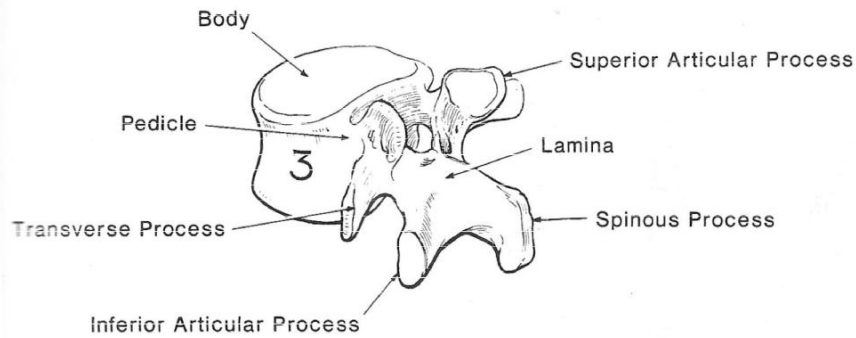


Figure 2: Components of a lumbar vertebra

Vertebral arch: surrounds and protects the spinal cord which is travel through the vertebral foramen. The vertebral arch consist of pedicles, lamina and the spinous process.

Pedicles are notched. The notched pedicle the adjacent vertebrae together to form an intervertebral foramen through which the spinal nerves emerge on either side. Lamina consist of a transverse process, superior and inferior articular processes which supports the artificial facets on each side.

Spinous process project backwards from the centre of the neural arch and forms an important palpable land mark for the anaesthesiologist.

Spinous process of the cervical vertebrae

The spinous process of the cervical vertebrae is short and bifid [with exception of C1 and C7] and is directed almost horizontally to the body of the vertebra.

Spinous process of the thoracic vertebra

The spinous process of the thoracic vertebra is long and is inclined at an angle of 45 to 60 degree to the body of the vertebra and the skin. So the needle should be directed at an angle of 45-60 degree cranially, to follow the upper border of the spine to enter the ligamentum flavum.

Spinous process of lumbar vertebra

The spinous process of the lumbar vertebra is directed horizontally backwards virtually 90° to the body of the vertebra and the skin. So the needle is to be directed perpendicular to the skin.

Intervertebral disc

Intervertebral disc lies between the vertebral bodies of the adjacent vertebrae. 25% of the length of spine is provided by the intervertebral disc. Intervertebral disc attaches to the hyaline cartilage of the adjacent vertebral body both above and below. Anteroposteriorly it attached to the anterior and posterior longitudinal ligaments.

Joints of the vertebral column

There are two joints in vertebral column. The intervertebral joints are located between adjacent vertebral bodies. They maintain the strength of attachment between vertebrae. The facet joints are formed between the articular processes.

Ligaments

The vertebrae are joined together by a series of ligaments and discs. Flexion, extension and rotation movements occur between the adjacent vertebrae but the individual joint movements are responsible for the flexibility of the vertebral column. Several ligaments give attachment to the vertebral column and provide stability and elasticity.

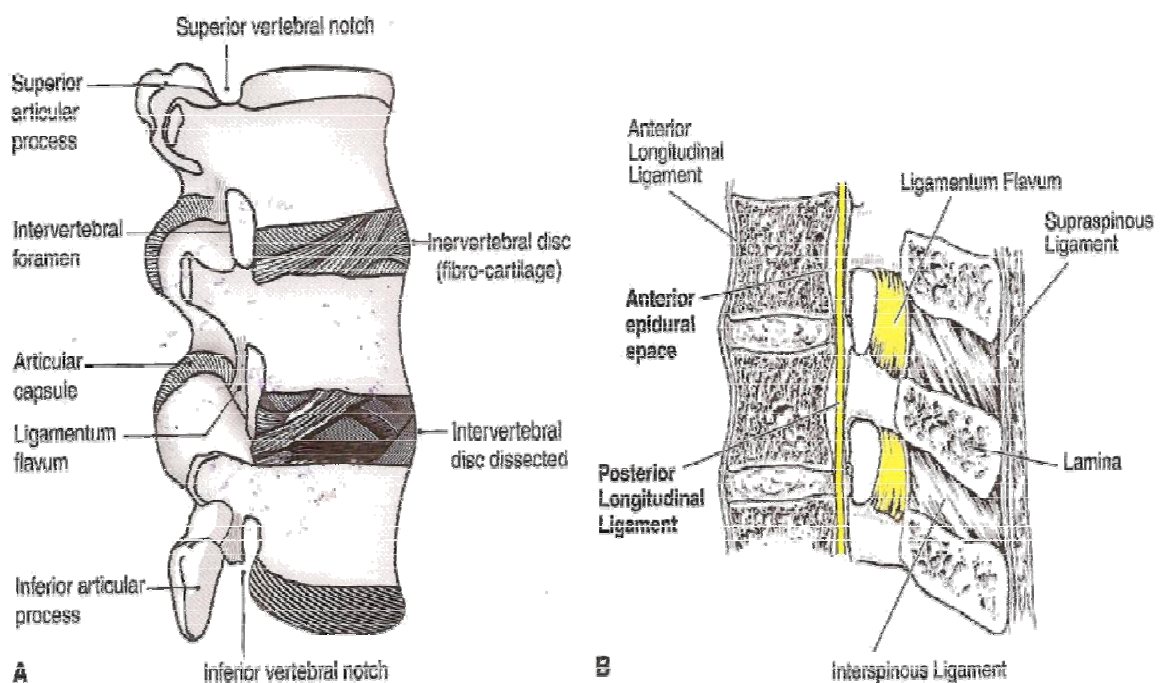


Figure 3: Ligaments of the lumbar vertebral column, shown in lateral view (A) and sagittal section (B)

Supraspinous ligament

The apices of the spinous processes from C7 To sacrum is connected by supraspinous ligament. It is a strong fibrous ligament. Above C7 it is continuous as ligamentum nuchae. In the lumbar region supraspinous ligament is broadest and thickest. It varies according to patient's age, sex and body build.

Interspinous ligament

Spinous processes are connected by interspinous ligament which is a thin membranous ligament that blending anteriorly with the ligamentum flavum and posteriorly with the supraspinous ligaments. Like supraspinous ligaments, the interspinous ligaments are thickest and broadest in the lumbar region.

Ligamentum flavum

It made up of elastic fibers. laminae of adjacent vertebrae is connected by ligamentum flavum. It extend above from caudal edge of vertebra to below upto cephaled edge of lamina. Laterally, this ligament begins at the roots of the articular processes and extends posteriorly and medially to the point where the laminae join to form the spinous process. Hence the two components of the ligament are limited, thus covering the interlaminar space. Because of its elasticity and its thickness of several millimeters in the lumbar region, the ligaments impart a characteristic 'springy' resistance, particularly to large bore needle with an upturned end [tuohy needle].

The ligament thickness, distance to dura and skin to dura distance vary with the area of vertebral canal.

Characteristics of ligamentum flavum at different vertebral level

Site	Thickness of ligament (mm)
Cervical	1.5 – 3.0
Thoracic	3.0 – 5.0
Lumbar	5.0 – 6.0
Caudal	2.0 – 6.0

Longitudinal ligament

Vertebral bodies are bind together by longitudinal ligament both anteriorly and posteriorly.

Epidural space

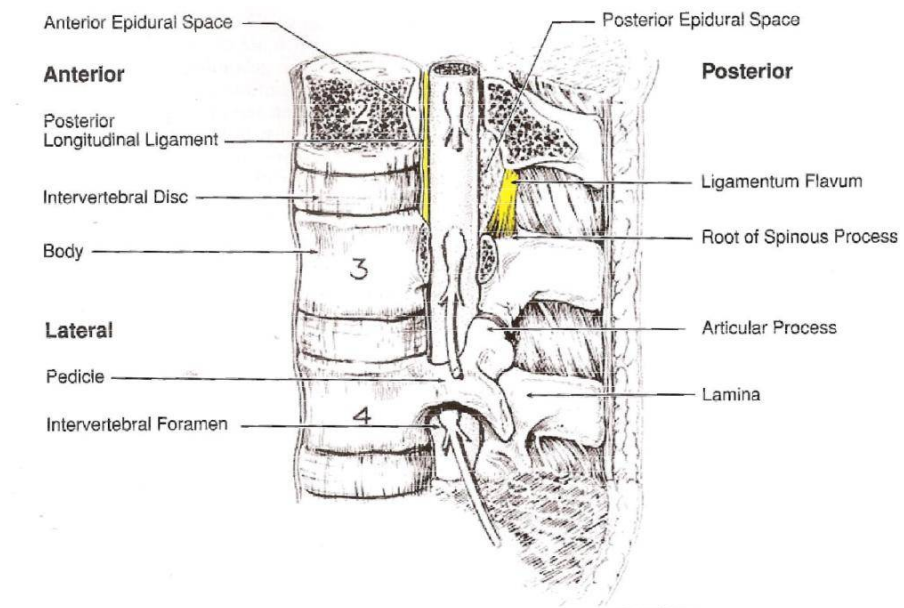


Figure 4: Boundaries of the epidural space

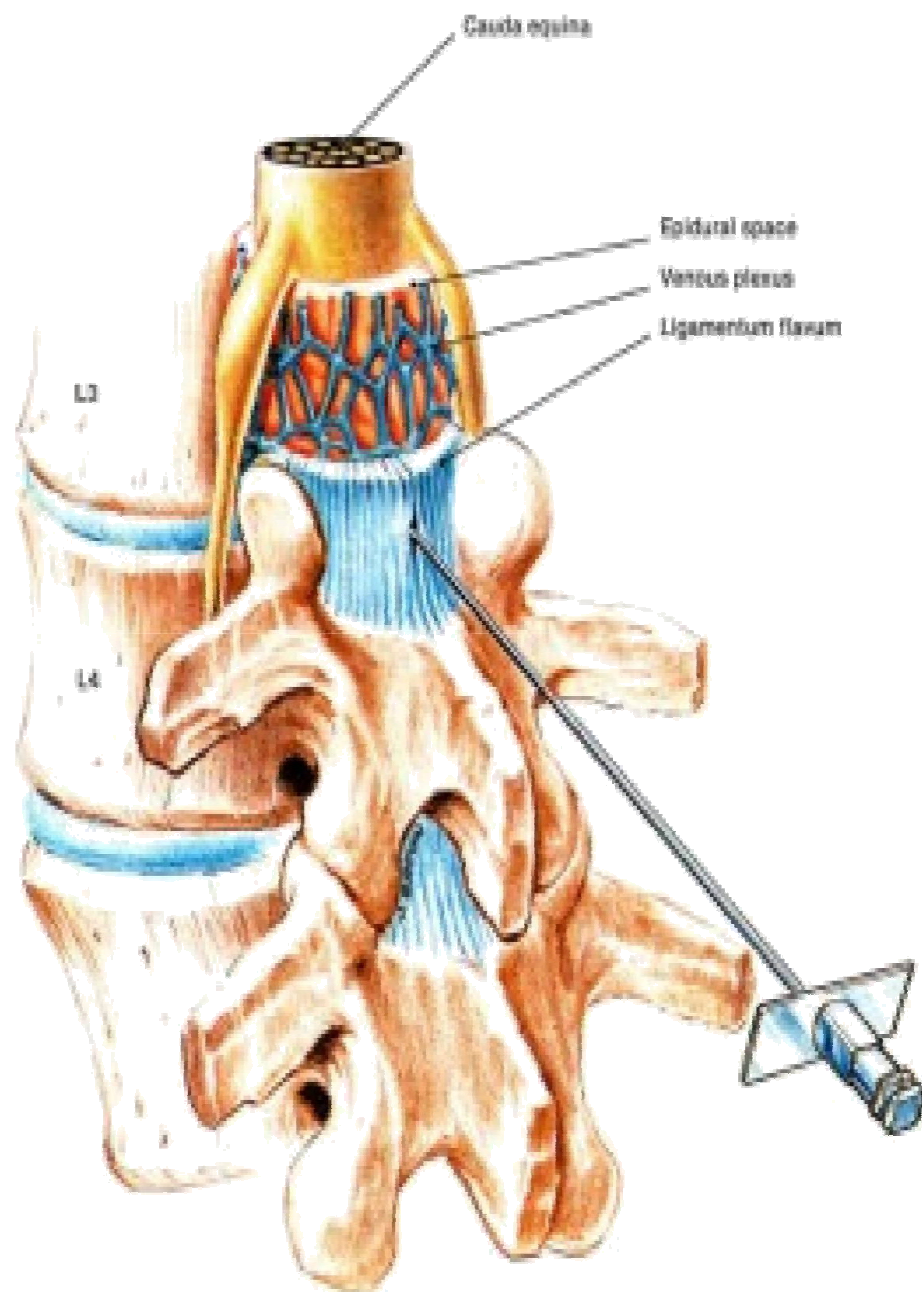


Figure 4: Boundaries of the epidural space

LOCATION: Between sides of the vertebral canal and spinal meninges

EXTENT:

Superior - Foramen magnum

Inferior - Sacral hiatus

Anterior - Posterior longitudinal ligament

Lateral - Pedicles and the intervertebral foramina

Posterior - Ligamentum flavum

WIDTH:

Narrow anteriorly and widest posteriorly

C5 Level - 1 to 1.5 mm

T6 Level - 2.5 to 3 mm

L2 Level - 5 to 6 mm (widest)

CONTENT OF EPIDURAL SPACE

Epidural space contains Batson plexus of veins, lymphatics, areolar tissue and nerve roots but no free fluid. So it is a potential space. Azygos veins in the thoracic and abdominal cavity and iliac vessels in the pelvic cavity are communicated with Batson plexus of veins. Batson plexus doesn't have valves, so blood from any of the connected system can flow into the epidural vessels and connect with intracranial veins. Air and drugs can accidentally enter into the brain through epidural veins. Except at the venous sinuses, no epidural spaces in the cranium because endosteal and meningeal dura are close together.

Epidural fat

Is semifluid lobulated areolar tissue extends throughout the spinal and caudal epidural space. It is most abundant posteriorly, diminishes adjacent to the articular processes, and increase laterally around spinal nerve roots, where it is continuous with the fat surrounding the spinal nerves in the intervertebral foramina and hence with the fat in the paravertebral space. Overall the amount of fat in the epidural space tends to vary in direct relation to that present elsewhere in the body, so that obese patients may have epidural spaces that are occupied by generous amount of fat. The fat itself has a great affinity for drugs with high lipid solubility, which may remain in epidural fat for longer periods. Uptake of local anaesthetics into epidural fat competes with vascular and neural uptake.

Epidural veins

The large valveless epidural veins are part of the internal vertebral venous plexus, which drains the neural tissue of the cord, the CSF and the bony spinal canal. The major portion of this plexus lies in the anterolateral part of the epidural space, out of reach of a correctly placed epidural needle.

The plexus has rich segmental connections at all levels with in the intervertebral foramina and the epidural space and within the body of the vertebrae. Superiorly, the plexus communicates with the occipital, sigmoid and basilar venous sinuses within the cranium. Inferiorly, anastomosis by way of the sacral venous plexus links the vertebral plexus to uterine and iliac veins.

By way of intervertebral foramina at each level, the vertebral plexus communicates with the thoracic and abdominal veins, so that pressure changes in these cavities are transmitted to epidural veins but not to the supporting bony elements of the neural arch and vertebral bodies.

Thus, marked increase in intra abdominal pressure may compress the inferior vena cava while distending the epidural veins, increasing flow upto the vertebrobasilar plexus. This increased flow is accommodated mostly by means of the azygous vein, which ascends in the right chest over the root of right lung into the superior vena cava.

Distension of epidural veins, owing to direct inferior vena cava obstruction [eg by the gravid uterus] or owing to increased thoracic and abdominal pressure, will also diminish the effective volume of the epidural space, with the result that injected local anaesthetic spread more widely up and down the epidural space.

Three important aspects of safety include:

1. The epidural needle should pierce the ligamentum flavum in the midline to avoid the laterally placed epidural veins.
2. Insertion of epidural needles or catheters or injections of local anaesthetics should be avoided during episodes of marked increase in size of epidural veins, such as that which occur with increased thoraco abdominal pressure during straining.
3. The presence of venacaval obstruction calls for a reduction in dose, a decrease rate of injection and increased care in aspirating of blood before epidural injection.

Spinal arteries

Spinal arteries are branches of aorta subclavian and iliac arteries. It crosses the epidural space at the region of dural cuff and enters into the epidural space. The anterior spinal artery territory supplying the anterior horn or motor area of the spinal cord is most vulnerable.

Epidural lymphatics

The dural cuff region is supplied with rich lymphatic network that rapidly conveys debris from arachnoid villi out through intervertebral foramina to reach lymph channels in front of the vertebral bodies.

Duralsac

Containing dura, arachnoid, spinal fluid, pia, spinal nerves and spinal cord is contained within the annular epidural space.

Dura

Outer most layers of the meninges is dura mater. It is the thickest membrane. It extends above from foramen magnum to below upto S2. Upper border of epidural space is formed by fused part of dura with periosteum, Dura mater fuses with filum terminale below. Laterally dura mater extends along with spinal nerve roots upto intervertebral foramen. Is the outermost and the thickest meningeal tissue. The dura mater is acellular. Blood vessels are rich in inner side of the dura mater. These blood vessels are responsible for the drug clearance when administered through subarachnoid and epidural space. Subdural space present between dura and arachnoid.

Arachnoid mater

The arachnoid mater is a delicate, avascular membrane. Arachnoid granulations are present in the epidural space which are formed by herniation of arachnoid through duramater. Material in the subarachnoid space leaves the CNS through arachnoid granulations.

Epidural pressure

In the lumbar region, the major cause of generation of a negative pressure lies in coning of the dura by the advancing needle point. Negative pressure increases as the needle advances across the epidural space towards the dura. Blunt needles with side openings produce the greatest negative pressure; they produce a good coning effect on the dura without puncturing it and transmit the negative pressure well because of their side opening.

Slow introduction of the needle produces the greatest negative pressure. Greatest negative pressure can be obtained if the dura is not distended [eg. By gravity in sitting position or by high abdominal or thoracic pressure]. In pregnancy, the epidural space may well have a positive pressure. Hence hanging drop technique may not be reliable in pregnant women to identify the epidural space.

Detection of epidural space

The methods for identification of the epidural space take the advantage of either the potential negative pressure or the sudden loss of resistance when the needle tip penetrates the tough ligamentum flavum.

Negative pressure techniques

1. Hanging drop technique of Gutierrez
2. Odom capillary tube method
3. Manometer method

Loss of resistance technique [described by Sicard, Forester and Dogliotti]

1. Syringe technique [using either normal saline or air]
2. Spring loaded syringe
3. Macintosh balloon technique
4. Brookes device
5. Vertical tube of dawkins

FACTORS AFFECTING EPIDURAL BLOCKADE

Many factors affect the efficacy, spread of blockade, fiber types blocked and other aspects of epidural blockade.

Site of injection and size of nerve roots

Epidural blockade is more intense and more rapid onset close to the injection site. L5 and S1 nerve roots are larger in size compared to other lumbar nerve roots. After lumbar epidural injection, there delay in the L5 and S1 segments.

Age

With advancing age, anatomic changes occur in the epidural space. In young individual, the areolar tissue around the intervertebral foramina is soft and loose.

In elderly areolar tissue becomes dense and firm, partially sealing the intervertebral foramina. With aging, the dura becomes more permeable to local anaesthetics because of significant increase in the size of the arachnoid villi.

The onset time to maximal caudal spread decrease with advancing age following epidural administration of bupivacaine. Bromage demonstrated that with age the epidural segmental dose requirement decreases in a linear way. The technique is technically difficult and hence there is always a chance of failure.

Height and weight

Height and weight of the patient doesn't influence the spread of epidural block.

Position

Comparison of sitting and lateral positions for epidural block reveals no significant difference in cephalad spread. Caudal spread of block in seated patients is slightly favoured by the sitting position.

Speed of injection

Speed of injection has little effect on spread of analgesia in epidural blockade.

But rapid injection of large volumes of solution may increase CSF pressure, decrease spinal cord blood flow, increase intracranial pressure and pose a risk of spinal or cerebral complications. Local anaesthetics should be injected into the epidural space slowly and preferably in incremental doses.

Volume, concentration and doses of local anaesthetics

Concentration of local anaesthetic has no role in spread of epidural blockade. Volume and dose of the drug are main determinants of both spread and quality of epidural blockade.

Higher the volume of local anaesthetics will produces more spread and more intense motor blockade. Higher the dose of local anaesthetics produces more intense sensory blockade and prolonged duration of epidural blockade. Higher concentration produces faster onset and more intense motor blockade.

Local anaesthetics

Duration of blockade differ between different local anaesthetics. Chloroprocaine provides shorter duration blockade, Lidocaine and Mepivacaine provides intermediate duration, and Bupivacaine, Ropivacaine and Etidocaine provides longer duration of epidural blockade. The differential capabilities of local anaesthetics to block sensory and motor fibers have been referred to as 'sensory motor dissociation'.

Epinephrine

Commonly added adrenergic agonist to local anaesthetic is Epinephrine in a doses of 5µg/ml [1:200000]. It prolongs the duration of lidocaine and mepivacaine epidural block upto 80%. Vasoconstrictors prolongs the duration of block by producing local vasoconstriction and thus decreased local anesthetic clearance from the epidural space. adrenaline produces inhibitory effect on motor and sensory neurons this is responsible for extended duration of motor and sensory blockade.

Number and frequency of local anaesthetics injections

Whether augmentation or diminution of neural blockade occurs after repeated epidural injection of local anaesthetics depends on the local anaesthetic agent, the number of injection and timing between injections.

Tachyphylaxis has been most clearly demonstrated in association with continuous epidural block in patients in whom repeated injections of the short acting amides – lidocaine, prilocaine or mepivacaine are used. The mechanism of tachyphylaxis is not known. It may be partly explained by pH changes in spinal fluid with repeated injections.

PHYSIOLOGICAL EFFECTS OF EPIDURAL BLOCKADE

With currently available local anaesthetic agents, spinal epidural neural blockade implies sympathetic blockade accompanied by somatic blockade, which may involve sensory and motor blockade alone or in combination. Some of the most important (but not all) of physiological effects of epidural blockade can be discussed in relation to either sympathetic blockade only of vasoconstrictor fibers (below T4) and or of cardiac sympathetic fibers.

Zone of differential blockade

Sensory

In intradural block sympathetic fibers are blockade two or three segments higher than sensory fibers. In extradural block, the relationship is complex. Level of sympathetic block is the same as (or lower than) sensory with epidural blockade. Sympathetic block will be greater when more concentrated solutions are used or when adrenaline added, as this has similar effect.

Motor

In intradural block, the difference between sensory and motor block is slight (two segments). In extradural block, the difference in levels is greater, depending very much on nature of local analgesic solution.

All types of nerve fibers are affected by local anaesthetics, faster preganglionic myelinated B fibers are more sensitive to local anaesthetics than slower post ganglionic non myelinated C fibers. Although A α sensory fibers and A β motor fibers have same conduction velocity, the former is more sensitive to blockade. This may be because of higher conduction frequency of sensory fibers. Sensory A α fibers conduct the nerve impulse at higher frequency so they are more sensitive to blockade than motor A β fibers, even though their conduction velocity is same. This may be because sensory fibers conduct at a higher frequency. It has been suggested that this selectivity for sensory fibers exhibited by Bupivacaine and Ropivacaine is a function of frequency dependent block, a property not shared by Etidocaine and Amethocaine.

Cardiovascular System

There are different ways in which intra and extradural spinal block can influence the cardiovascular system.

1. Vasodilatation of resistance and capacitance vessels. Block of cardiac efferent sympathetic fibers from T1 and T4 resulting in loss of chronotropic and Inotropic drive and fall in cardiac output.
2. The arterial or Bainbridge reflex causing bradycardia.
3. The operation of Marey's law causing tachycardia.

4. Depression of vascular smooth muscle and β adrenergic blockade of myocardium with fall in cardiac output.
5. Adrenaline effect (if used) following absorption, resulting in β stimulation and associated rise in cardiac output and reduction in peripheral resistance.

The overall effect is likely to be greater fall in mean arterial pressure than if adrenaline had not been used. Block not extending above T4 is not always associated with fall of blood pressure in fit young adults although the elderly many suffer significant hypotension when moderate volumes are injected into the epidural space. Corrective measures may be considered if arterial pressure falls more than 1/3 below its pre-operative level.

Slowing of heart rate is caused if any of the anterior roots carrying sympathetic cardiac accelerator fibers are blocked, as may happen in higher spinal blockade above T4, T5. A further cause of slow pulse rate is the lowering of blood pressure in the right atrium consequent on diminished venous return [Bainbridge (1874-1921) effect]. On the other hand, Tachycardia during spinal analgesia may result from the operation of Marey's Law (a pulse of low tension is fast). Bradycardia is the more frequent effect.

Theories of causation of fall in blood pressure

1. Diminished cardiac output consequent on reduction of venous return to heart, and lack of muscular propulsive force on veins.
2. Dilatation of post arteriolar capillaries and small venules due to paralysis of vasoconstrictors, compensatory vasoconstriction takes place in areas not anaesthetized via carotid sinus reflexes. In high spinal blocks, majority of vasoconstrictor fibers including those to arm [T2-T10], are paralyzed, hence low blood pressure. Total peripheral resistance decreases by only 18% following complete sympathetic block in healthy young adults.
3. Paralysis of sympathetic nerve supply to heart T1-T4. Bradycardia may give rise to fall in cardiac output.
4. Paralysis of sympathetic nerve supply to adrenal glands splanchnic nerves, with consequent catecholamine depletion
5. Absorption of drug into circulation. This is more likely to be a cause of hypotension after extradural than after intradural analgesia because of the large amount of analgesic drug injected.
6. Ischemia and hypoxia of vital centers

7. Hypovolemia, if present, may give rise to fall in blood pressure if central neural blockade is employed.
8. Compression of great vessels within abdomen, by the pregnant uterus, abdominal tumours or abdominal packs may cause severe hypotension in presence of central neural blockade.

Respiratory system

Anterior roots of C3, C4, C5 form phrenic nerve which supplies diaphragm and should not be encroached on in SAB but phrenic nerve paralysis can occur. Medullary ischaemia or toxic effect of drug in extradural block can cause apnea. Motor blockade during spinal anaesthesia and reduction of sensory input to respiratory center causes quiet and tranquil breathing. Pre existing pulmonary congestion is relieved by reduced arterial and venous tone which reduces work of heart. Extradural block does not alter V/Q ratio or FRC much. Pulmonary gas exchange is preserved.

The effect of block is largely on cardiovascular system. Vital capacity and force expiratory volume may be reduced, especially in cigarette smokers. Descent of diaphragm occurs due to relaxation of abdominal wall muscle. Paralysis of Intercostals muscle is compensated by descent of diaphragm.

This not accompanied by hypoxia and hypercapnia although the ability to cough forcibly to expel secretion is impaired.

The patient may stop breathing so that respiratory support by IPPV and, if necessary the tracheal intubation required. Causes may be:

- Inadequate medullary blood flow due to inadequate cardiac output-a serious situation demanding immediate cardiorespiratory support.
- Total spinal analgesia with denervation of all respiratory muscles. True phrenic nerve paralysis is uncommon because all motor roots are large and analgesic solution is likely to be weak when it reaches the cervical region.
- Massive epidural spread.
- Accidental subdural injection
- Toxic effects of local anaesthetic drug.
- Injecting narcotic analgesic drugs

Gastrointestinal system

The esophagus is innervated by vagus and is not affected by inhibitory preganglionic sympathetic fibres from T5 –L1. As vagus is powerful, the removal of sympathetic impulses causes small gut contraction and sphincter relaxation and active peristalsis although not more frequent. Intra luminal pressure in bowel is increased.

Nausea and vomiting due to the hypotension may occur and usually come on in waves-lasting a minute or so and then passing away spontaneously.

Stimuli arising in the upper abdomen may ascend along the unblocked vagi and perhaps the phrenic nerve, and cause discomfort, if the patient is conscious. Infiltration of local anesthetic solutions may prevent this by blocking vagal afferents. Blood supply to colon and oxygen availability are increased, to prevent the anastomotic leakage following gut resection.

Theories of causation of nausea and vomiting:

1. Hypotension, correction using a pressor drug may relieve nausea
2. Increased peristalsis of the gut causes nausea and vomiting
3. Handling of vagal nerve endings and plexuses, during surgery.
4. Relaxation of pylorus and sphincter of bile duct cause collection of bile in the stomach.
5. Opioid premedication
6. Psychological factors
7. Hypoxia

Gastric emptying time is quicker when extradural block is employed for postoperative pain relief than when narcotic analgesics are used.

Liver

Blood supply to liver is reduced according to mean arterial pressure. but it is clinically insignificant. Liver disease may interfere with the metabolism of local anaesthetic drugs.

Endocrine system

The usual increase of ADH during surgery is suppressed. Spinal block delays adrenal response to trauma, whereas operations under general anaesthesia cause a rise in steroids.

In any case, either regional or general, there is no difference in the postoperative period once the effects of the block are discontinued. Surgical stress causes hyperglycemia which is prevented by central neuraxial blockade. This effect is beneficial in diabetic patient. there is a chance of hypoglycemia in diabetic patient due to augmentation of insulin effect.

Extradural block prevents lymphopenia and granulocytosis after operation, thus inhibiting the metabolic endocrine response to surgery and preventing immune depression.

Genito urinary system

Sympathetic innervation of kidney is from T11 to L1 through the lowest splanchnic nerves. Blood flow to the kidney is autoregulated. It is impaired when mean arterial pressure is reduced below 50mm Hg.

Blood supply to the kidney is normal once the blood pressure is return to normal. Sphincters of bladder are not relaxed, so soiling of table by urine is not seen and tone of ureters is not greatly altered. Blockade of nervi erygentes [S2 and S3] causes engorgement of penis. This is one of the positive sign of successful neuraxial blockade. Retention of urine occur due to blockade of autonomic nerve fibers responsible for bladder emptying.

Body temperature

Heat loss occur due to vasodilatation in hot environment increased in body temperature occur due to loss of sweating. Catecholamine secretion is reduced in central neuraxial blockade so reduction in metabolism causes less heat loss.

Extradural space is a temperature sensitive zone, whereas intradural space is not. Cold solutions injected into extradural space may induce shivering

1. Because the large veins act as exchangers.
2. As a result of sensory input.
3. Possibly because of the existence of thermal sensors.

PHARMACOLOGY OF ROPIVACAINE

Ropivacaine is a long acting local anaesthetic. Bupivacaine is a racemate mixture, Ropivacaine is a pure S (-) enantiomer. Ropivacaine is less cardiotoxic than bupivacaine.

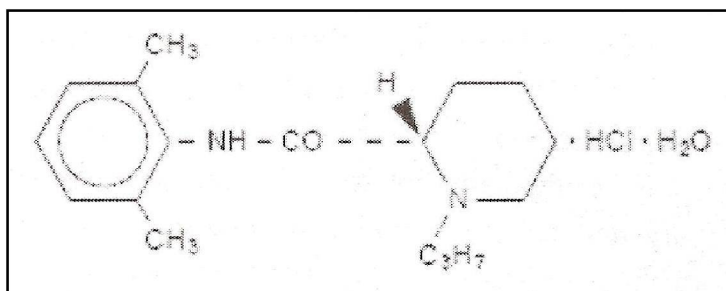
Chemical structure

Ropivacaine is a hydrochloride salt of 1-propyl-2', 6'-pipecoloxylidide.

Physiochemical properties

Molecular weight	- 328.89 274 (base)
Pka	- 8.1
Plasma protein binding	- 94%
Lipid solubility	- 2.9

Structural formula



Mechanism of action

Mechanism of action of ropivacaine is inhibition of sodium ion influx in reversible manner. Sodium channel inhibition is augmented by potassium channel blockade. Less lipophilic property of ropivacaine is responsible for poor penetration of ropivacaine into large myelinated fibers.

Like other local anaesthetics, ropivacaine elicits nerve block via reversible inhibition of sodium ion influx in nerve fibers. Ropivacaine has selective action on A δ and C nerves which are pain transmitting, less effect on A β fibers, which are responsible for motor function.

Pharmacodynamics

CNS and cardiovascular effects

Cardiovascular and CNS toxicity of ropivacaine occur at high plasma concentration or due to accidental intravascular injection.

Less lipophilicity and stereoselective property of ropivacaine is responsible for less cardiac and CNS toxicity

During accidental intravascular injection CNS toxicity occurs prior to CVS toxicity. Changes in Cardiac contractility, conduction time and QRS width are smaller in ropivacaine compared with bupivacaine.

Other effects

At concentrations of 3.75 and 1.88 mg/ml, ropivacaine inhibits platelet aggregation. Antibacterial property of ropivacaine is responsible for inhibition of bacterial growth in vitro.

Pharmacokinetic properties

Absorption and distribution

Route of administration, dose of drug, hemodynamic status of the patient and blood supply of the injection site influences plasma concentration of the drug.

Initial phase half life of the ropivacaine is 14mins. slower phase half life is 4.2 hours.

Ropivacaine binds to α_1 - acid glycoprotein upto 94%. During LSCS epidurally administered Ropivacaine crosses the placenta.

Volume of distribution of intravascularly administered ropivacaine is 41L. Addition of adrenaline to ropivacaine enhances the analgesic property of the latter drug by reducing vascular absorption of drug.

Metabolism and elimination

Metabolism of ropivacaine takes place in liver. Hydroxylation of ropivacaine to 3'-hydroxy Ropivacaine by CYP450. Excretion of ropivacaine upto 86% by kidneys.

Relative potency

Lipid solubility of the ropivacaine decides its potency and toxicity. At higher doses Ropivacaine has similar potency to bupivacaine, at smaller doses Ropivacaine is less potent than bupivacaine.

Tolerability- In adults

Tolerability of ropivacaine is not dependent on route of administration. Dose dependent adverse effects occur if ropivacaine is given through epidurally.

In old age cardiovascular toxicity occurs when ropivacaine is given in higher doses.

In children

Regardless of the route of administration of drug Ropivacaine is well tolerated by children aged from 1 month to 15 yrs. In children nausea and vomiting occur more frequently.

In exposed fetuses and neonates

Fetal bradycardia and neonatal jaundice occur when fetus is exposed to ropivacaine.

Drug interaction

Ropivacaine when used with other amide local anaesthetic produces additive effect and more toxicity.

Drugs which inhibit the CYP450 reduce the metabolism of ropivacaine and increase its plasma concentration.

Dosage

Dose of Ropivacaine depends on the type of procedure, the area to be anaesthetized, the blood supply of the tissue, amount of neuronal segments to be blocked, the depth of anaesthesia and degree of muscle relaxation, individual tolerance and physical condition of the patient.

Clinical applications

Epidural administration

Epidural administration of ropivacaine, provides effective surgical anaesthesia.

a. Cesarean section

Efficiency of ropivacaine is similar to bupivacaine regarding to onset of motor and sensory blockade.

b. Hip or lower limb surgery

Epidurally administered ropivacaine for lower limb and hip surgery, efficiency is similar to bupivacaine and levobupivacaine.

Intrathecal administration

Intrathecaly administered ropivacaine is less potent than bupivacaine.

Peripheral nerve blocks

Site of injection governs the onset and spread of ropivacaine when administered for Peripheral nerve blocks. 0.5% or 0.75% of ropivacaine administered for brachial plexus block provides prolonged motor and sensory blockade compared to bupivacaine. 0.75% of ropivacaine produces faster onset of motor and sensory blockade. In lower limb surgeries where sciatic or combined femoral and sciatic block was given, Ropivacaine 0.75% had significantly faster onset of sensory and motor block than 0.5% bupivacaine.

Management of postoperative pain

Lower doses of local anaesthetics are generally required for postoperative pain relief than for anaesthesia. Post operative pain relief can be provided by Epidural administration Peripheral nerve blocks Local infiltration, instillation and intra articular administration.

Management of labour pain

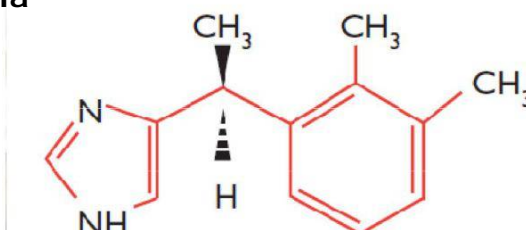
Labour pain effectively relieved by ropivacaine when administered epidurally.

Ropivacaine administered Intrathecally for combined spinal epidural anaesthesia produces rapid pain relief during labour and reduced motor blockade.

PHARMACOLOGY OF DEXMEDETOMIDINE

Dexmedetomidine hydrochloride, an imidazole compound is the pharmacologically active s-enantiomer of medetomidine, a veterinary anaesthetic agent. It is described chemically as (+)-4-(s)[2 3-(dimethylphenyl) ethyl]-11 H-imidazole monohydrochloride. Its empirical formula is $C_{13}H_{16}N_2HCl$ and its molecular weight is 236.7.

Structural formula



Chemical structure of dexmedetomidine

PHYSIOCHEMICAL PROPERTIES

A white or almost white powder that is freely soluble in water with Pka of 7.1. Partition coefficient in octanol: water at pH 7.4 is 2.89. Preservative free dexmedetomidine is available in 0.5ml, 1ml and 2 ml ampoules as Dexmedetomidine Hydrochloride for intravenous use (Dexem, Themis Medicare Ltd., 200 g/ml).

It can also be used for intrathecal and epidural anaesthesia.

MECHANISM OF ACTION OF DEXMEDETOMIDINE

The affinity of dexmedetomidine towards α_2 receptors is 8 times more than that of clonidine. The binding ratio of dexmedetomidine towards α_1 : α_2 is 1:1620. Antagonist of α_2 receptors (atipamezole) reverses the effects of dexmedetomidine.

The pharmacodynamic effects of Dexmedetomidine are mediated by α_2 receptor subtypes. Neuroprotection, sedation, hypnosis, sympatholysis, analgesia, and inhibition of insulin secretion are mediated by α_{2a} receptors.

Analgesia, vasoconstriction in peripheral arteries and suppression of shivering are mediated by α_{2b} receptors.

The modulation of cognition, sensory processing, mood and regulation of epinephrine outflow from the adrenal medulla are mediated by α_{2c} receptors.

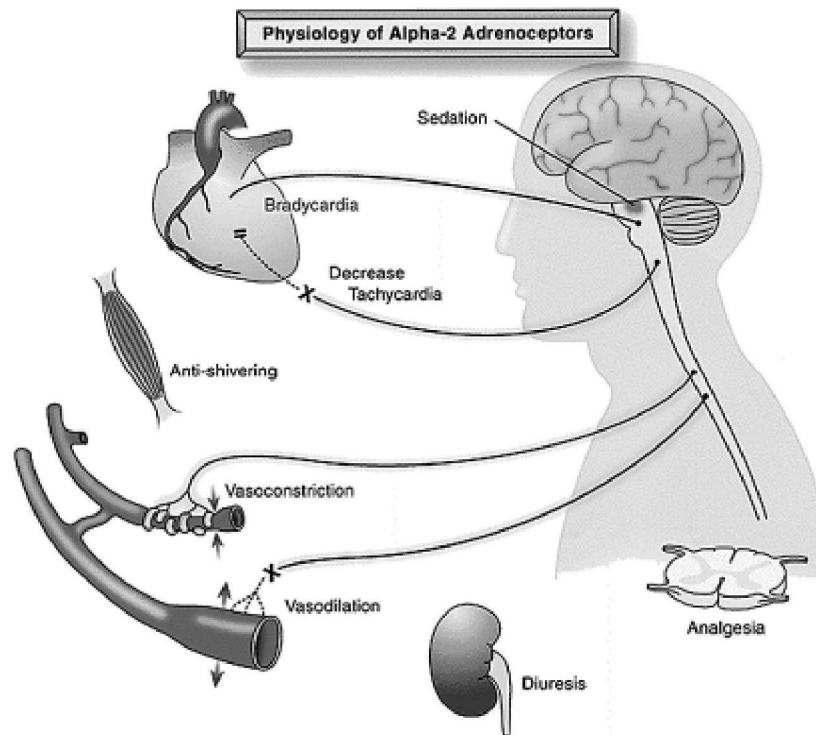


Figure 5: Responses that can be mediated by α -2 adrenergic receptors

In CNS Alpha-2 adrenoceptors are more in locus ceruleus and in brainstem. Presynaptic activation of alpha-2A adrenoceptor in the locus ceruleus inhibits the release of nor-epinephrine and results in the sedative and hypnotic effects. In addition, the locus ceruleus is the site of origin for the descending medullospinal nor adrenergic pathway, known to be an important modulator of nociceptive neurotransmission. Stimulation of alpha-2 adrenoceptors in this area terminates the propagation of pain signals leading to analgesia. Postsynaptic activation of alpha-2 receptors in the CNS results in decrease in sympathetic activity leading to hypotension and bradycardia.

Alpha 2 receptors present in the dorsal horn of spinal cord. Activation of alpha 2 receptors causes inhibition of neurons responsible for pain and reduces substance p release. Also the alpha-2 adrenoceptors located at the nerve endings have a possible role in the analgesic mechanism by preventing nor epinephrine release. The spinal mechanism is the principal mechanism for the analgesic action of Dexmedetomidine even though there is a clear evidence for both a supraspinal and peripheral sites of action.

Pharmacodynamics of dexmedetomidine

Dexmedetomidine is considered as the full agonist at alpha-2 receptors compared to clonidine which is considered as a partial agonist at alpha-2 adrenoceptors. The selectivity of Dexmedetomidine to alpha-2 receptors compared to alpha-1 receptors is 1620:1, where as with clonidine it is 200:1. The selectivity is dose dependant, at low to medium doses and on slow infusion, high levels of alpha-2 selectivity is observed, while high doses or rapid infusions of low doses are associated with both alpha-1 and alpha-2 activities.

Central nervous system

1. Sedation, anxiolysis, hypnosis and amnesia

Sedation and anxiolysis produced by dexmedetomidine in dose dependant manner.compared to midazolam and propofol dexmedetomidine produces unique quality of sedation. Correlation between BIS value and sedation is good.patient can be arousable even at deeper level of sedation.sedation induced by dexmedetomidine is like normal sleep. Activation of GABAnergic neuron in ventrolateral preoptic nucleus and inhibition of noradrenergic neuron in nucleus cereleus is mediated by Stimulation of alpha-2A receptors.

The participation of non-rapid eye movement sleep pathways seems to explain why patients who appear to be deeply asleep from Dexmedetomidine are relatively easily aroused in much the same way as occurs with natural sleep. This type of sedation is branded "cooperative or arousable", to distinguish it from sedation induced by drugs acting on the GABA system, such as midazolam or propofol which produce a clouding of consciousness. Sedation with Dexmedetomidine is dose dependant, however even low doses might be sufficient to produce sedation. Dexmedetomidine may lack amnestic properties but amnesia is achieved with dexmedetomidine only at high plasma levels (>1.9 ng/ml) without retrograde amnesia.

2. Analgesia

Analgesic effect of Dexmedetomidine is mediated through both supraspinal and spinal cord level. appears to exert analgesic effects at the spinal cord level and at supraspinal sites. Analgesic property of dexmedetomidine also mediated through non spinal mechanism.

Dexmedetomidine administered through intra articular route provide better analgesia for knee surgeries compared to IV route. Blockade of C and A δ fibres and release of enkephalin. is mediated by stimulation of alpha 2A fibers.

Respiratory effects

Dexmedetomidine is able to achieve its sedative, hypnotic and analgesic effects without causing any clinically relevant respiratory depression unlike opioids. The changes in ventilation appeared similar to those observed during natural sleep. Dexmedetomidine do not cause any changes in arterial oxygenation, pH and respiratory rate. It also exhibited a hypercarbic arousal phenomenon, which has been described during normal sleep and is a safety feature. The obstructive respiratory pattern and irregular breathing seen with high doses of 1-2 μ g/kg given over 2 minutes and are probably related more to deep sedation and anatomical features of the patient and this could be easily overcome by insertion of an oral airway.

Co-administration of dexmedetomidine with anaesthetic agents, sedatives, hypnotics or opioids is likely to cause additive effects. Intravenous or inhaled Dexmedetomidine has been implicated in blocking histamine induced bronchoconstriction in dogs.

Dexmedetomidine is effective in achieving excellent sedation without respiratory depression during fibreoptic intubation or other difficult airway procedures. Intubating conditions are further enhanced because Dexmedetomidine decreases saliva production and airway secretions.

Cardiovascular effects

Dexmedetomidine does not appear to have any direct effects on the heart. A biphasic cardiovascular response has been described after the application of dexmedetomidine. The administration of a bolus of 1 µg/kg body weight, initially results in a transient increase of the blood pressure and a reflex decrease in heart rate, especially in young healthy patients. The initial reaction can be explained by the peripheral alpha 2B adrenoceptors stimulation of vascular smooth muscles and can be attenuated by a slow infusion over 10 or more minutes. Even at slower infusion rates however the increase in mean arterial pressure over the first 10 minutes was shown to be in the range of 7% with a decrease in heart rate between 16% and 18%.

The initial response lasts for 5-10 minutes and is followed by a decrease in blood pressure of approximately 10%-20% below baseline values; central sympatholytic property of dexmedetomidine is responsible for most of its action. Reduction in release of nor epinephrine is responsible for dexmedetomidine mediated decrease in heart rate.

The baroreceptor reflex and pressor stimuli mediated increase in heart rate are not affected by dexmedetomidine.

High doses of dexmedetomidine produce bradycardia and hypotension which are treated by atropine, ephedrine and volume infusion.

Effect on adrenocorticotrophic hormone (ACTH) secretion

At higher doses and prolonged uses of dexmedetomidine produce reduction in cortisol's response to ACTH.

Effect on renin release

β -adrenoceptor activation increases renin release. Renin release is inhibited by α -2 adrenoceptor stimulation.

Effect on thermoregulation

Reduction of vasoconstriction and shivering threshold produced by dexmedetomidine. α 2b receptors located in the thermoregulatory centre of hypothalamus. Dexmedetomidine act on α -2 receptors and reduces shivering.

Effects on renal function

Action of vasopressin at collecting duct is inhibited by dexmedetomidine, results in reduced expression of aquaporin 2 and reduced water and salt absorption.

Organ protective effects

Reduction in heart rate and blood pressure promotes the cardio protective property of dexmedetomidine. neuroprotective property of dexmedetomidine is mediated by reduction of cerebral blood flow, reduction of reperfusion injury, and inhibition of sympathetic system.

Pharmacokinetics

Onset of action -15mins

Peak plasma level-60 mins

Distribution half life -6mins

Elimination half life-2-3 hours

Volume of distribution-1.3l/kg

Protein binding -94%

Context sensitivity half time-4mins after 10 mins of infusion
250 mins after 8hrs infusion.

Bioavailability-73-88%

Perioperative uses of Dexmedetomidine

1. Premedication

Dexmedetomidine used as premedication because of its sympatholytic, analgesic, anxiolysis, and hypnotic property.

As a premedicant, Dexmedetomidine, at IV doses 0.33 to 0.67µg/kg given 15 minutes before surgery, seems efficacious, while minimizing the cardiovascular side effects of hypotension and bradycardia.

- a. It reduces thiopental requirements.
- b. Reduces the requirements of volatile anaesthetics.
- c. More effectively attenuates the haemodynamic responses to endotracheal intubation.
- d. Decreases plasma catecholamine concentrations.
- e. Improves perioperative haemodynamic and sympathoadrenal stability.

2. Use of dexmedetomidine for regional anaesthesia

- a. Epidural dexmedetomidine at a dose of 100µg decreased the incidence of postoperative shivering.
- b. Intrathecal dexmedetomidine at a dose of 3µg causes significant prolongation of sensory and motor blockade.
- c. Addition of 0.5µg/kg body weight of dexmedetomidine to lidocaine for intravenous regional anaesthesia improves the quality of anaesthesia and perioperative analgesia.

4. Use in monitored anaesthesia care (MAC):

Dexmedetomidine produces analgesia, arousable sedation without respiratory depression made its use in monitored anaesthesia care.

4. Dexmedetomidine has also been used as sole anaesthetic agent upto doses of 10µg/kg/hr.

5. Use of dexmedetomidine in postoperative period:

dexmedetomidine can be used in spontaneously breathing patients. The ongoing sedation and sympatholytic effects are beneficial in reducing postoperative myocardial ischemic events in high risk patients undergoing non-cardiac surgery.

6. Use of dexmedetomidine in paediatric age group – addition of dexmedetomidine 2µg/kg body weight to bupivacaine for caudal analgesia promotes analgesia after anaesthetic recovery without increasing the incidence of side effects.

7. Use of dexmedetomidine in intensive care unit (ICU): it provides adequate sedation with minimal respiratory depression and can be used for weaning patients from ventilator.

Adverse effects

Other side effects of dexmedetomidine other than hypotension and bradycardia are hypertension after loading dose, dystonic movements, atelectasis, nausea and vomiting, dry mouth, tachycardia, atrial fibrillation, haemorrhage, acidosis, confusion, agitation and rigors which are rare. Withdrawal phenomenon is reported after abrupt discontinuation with prolonged administration of dexmedetomidine, leading to development of hypertension, tachycardia, emesis, agitation, dilated pupils, diarrhea, and increased muscle tone and tonic clonic seizures.

Dosage and administration

The recommended Dexmedetomidine dose is an IV infusion bolus of 1 µg/kg body weight over a 10 minute period, followed by a continuous IV infusion of 0.2-0.7 µg/kg/hr. The maintenance dose is titrated until the sedation goal is reached.

It is not necessary to discontinue Dexmedetomidine before, during or after extubation. Dose up to 2.5µg/kg/hr for up to seven days, with no rebound effect on withdrawal and no compromise in haemodynamics stability have been used in clinical trials.

Drug interactions

Dexmedetomidine has shown to inhibit CYP2 D6 in vitro, but the clinical significance of this inhibition is not well established. Dexmedetomidine appears to have little potential for interactions with drugs metabolized by the cytochrome p450 system.

Co-administration of Dexmedetomidine with sevoflurane, isoflurane, propofol, alfentanil and midazolam may result in enhancement of sedative, hypnotic or anaesthetic effects.

REVIEW OF LITRATURE

Saravia P.S.F, Sabbag AT et al in 2008 conducted a double blind, controlled study on 40 patients belonging to ASA 1 and 2 undergoing surgery on a hernia or abdominal wall, varicose vein of the lower limbs to evaluate the clinical characteristics of epidural anaesthesia performed with ropivacaine associated with dexmedetomidine.

Author concluded that dexmedetomidine at a dose of 1 µg/kg, acts synergistically with 0.75% ropivacaine in epidural anaesthesia. It increases the duration of analgesia, motor block intensifies and prolongs the duration of post-operative analgesia, without increased morbidity.

Lopez SAO, Sanchez KAM et al in 2008 conducted a descriptive, prospective study on 40 ASA1 and 2 patients posted for surgery on abdomen and lower limbs to evaluate the effects of epidural dexmedetomidine in regional anesthesia to reduce anxiety. Authors concluded that the use of dexmedetomidine by peridural route at 1 µg/kg dose plus local anesthetics is an alternative to achieve an anesthetic quality that enables to keep the patient in a state of active sedation, which reduces the likelihood of respiratory depression, which can arise when adjuvant drugs are administered intravenously.

It also reduces the doses of local anesthetics, as it potentiates the effects of both drugs, with consequent reduction of their adverse effects.

Bajwa SJ, Arora V, Kaur J et al 2011 conducted a randomized controlled study on 100 patients to evaluate the effect of epidural dexmedetomidine and fentanyl epidural analgesia in lower limb orthopaedic surgeries.

Authors concluded that dexmedetomidine is a better alternative to fentanyl as an epidural adjuvant as it provides comparable stable hemodynamics, early onset and establishment of sensory anesthesia, prolonged post operative analgesia, lower consumption of post-op LA for epidural analgesia; and much better sedation levels.

Wahlander S, Frumento RJ et al in 2005 conducted a study to test the hypothesis that after thoracic surgery, the supplementation of a low-dose thoracic epidural (ED) bupivacaine (0.125%) infusion followed by intravenous (IV) dexmedetomidine decreases the analgesic requirement without causing respiratory depression. The primary endpoint was the need for additional ED bupivacaine administered through patient-controlled epidural analgesia (PCEA). Secondary endpoints included the requirement for supplemental opioids and the impact of dexmedetomidine on CO₂ retention.

The authors concluded that in postthoracotomy patients, IV dexmedetomidine is a potentially effective analgesic adjunct to thoracic ED bupivacaine infusion and may decrease the requirement for opioids and potential for respiratory depression.

Coskuner I, Tekin M et al in 2007 conducted a study on 60 ASA 1 and 2 patients to evaluate the effects of intravenous dexmedetomidine on the duration of anaesthesia, level of wakefulness and respective side effects in bupivacaine-induced epidural anaesthesia.

Authors conclude that intravenous administration of dexmedetomidine prolonged the duration of epidural anaesthesia, provided sedation and had few side-effects.

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Hennawy AME, Elwahab AMAet al in 2009 conducted a double-blind randomized study on sixty patients (6 months to 6year) posted for lower abdominal surgeries to evaluate the analgesic effects and side effects of dexmedetomidine and clonidine added to bupivacaine.

Authors concluded that addition of dexmedetomidine or clonidine to caudal bupivacaine significantly promoted analgesia in children undergoing lower abdominal surgeries with no significant advantage of dexmedetomidine over clonidine and without an increase in incidence of side effects.

Elhakim M, Abdelhamid D et al in 2010 conducted a randomized controlled study on 50 adult male patients to evaluate the effect of epidural dexmedetomidine on intraoperative awareness and post-operative pain after one-lung ventilation.

Authors concluded that in thoracic surgery with one lung ventilation, the use of epidural dexmedetomidine decreases the anaesthetic requirements significantly, prevents awareness during anaesthesia and improves intraoperative oxygenation and post-operative analgesia.

Bajwa SJ, Bajwa SK, Kaur J et al in 2011 conducted a prospective randomized double blind study on 50 adult female patients aged between 44 and 65 years of ASA 1 and 2 patients who underwent vaginal hysterectomies to compare the effect of dexmedetomidine and clonidine in epidural anaesthesia. Patients with haematological disease, bleeding or coagulation test abnormalities, psychiatric diseases, diabetes, history of drug

abuse and allergy to local anaesthetics of the amide type were excluded from the study.

Author concluded that dexmedetomidine is a better adjuvant than clonidine in epidural anaesthesia as far as patient comfort, stable cardio-respiratory parameters, intra-operative and post-operative analgesia is concerned and provides superior sedative and anxiolytic properties during the surgical procedure under regional anaesthesia.

Sinha S, Mukherjee M et al in 2012 studied the analgesic efficacy of ropivacaine with ropivacaine plus dexmedetomidine for paravertebral block in unilateral renal surgery.

Authors concluded that addition of dexmedetomidine to local anaesthetic agent ropivacaine significantly prolongs the duration of analgesia in paravertebral blocks without causing significant haemodynamic instability. Also co administration of dexmedetomidine leads to decreased total consumption of ropivacaine which is very beneficial for renal compromised patients.

Brummett CM, Norat MA et al in 2013 conducted a study to test the hypothesis that high-dose dexmedetomidine added to local anesthetic would increase the duration of sensory and motor blockade in a rat model of sciatic nerve blockade without causing nerve damage.

METHODOLOGY

A study entitled "Comparative study of Epidural 0.75% Ropivacaine with Dexmedetomidine and 0.75% Ropivacaine alone in lower limb surgeries" was undertaken in Government Rajaji hospital, Madurai from October 2014 to July 2016. After getting hospital ethical committee and informed consent the study was done. 100 patients, posted for elective lower limb surgeries belonging to ASA class I and II were included in this study.

The study patients randomly divided into two groups with 50 patients in each group.

1. **Group R (Number of patient-50)** - 15ml of 0.75% ropivacaine (Ropivacaine 0.75% preservative free – ROPIN 0.75% 20 ml ampoules – Neon laboratories India limited).

2. **Group RD (Number of patient-50)** - 15ml of 0.75% ropivacaine + 0.6µg/kg of dexmedetomidine

(inj.DEXTOMID-1ml=100mcg, 1ml ampoule)

Inclusion criteria for the study

- Age of the patient between 18 to 65 years
- Both sex.
- ASA class I and II patients posted for elective lower limb surgeries
- Weight more than 50 kgs
- Height between 150-180cms

Exclusion criteria for the study

- Patient not willing for regional anaesthesia.
- Pregnant and lactating women.
- Emergency surgical procedures.
- Obese patient with BMI more than 30.
- Patients with
 - increased intracranial pressure
 - hypovolemia
 - Abnormal coagulation profile
 - Infection at injection site
 - uncorrected hypertension/ diabetes mellitus
 - CNS disorder and spinal deformity
 - cardiac disease
 - hepatic disease
 - allergy to ropivacaine and dexmedetomidine

pre-anaesthetic assesement

- History and general examination of the patient
- Assessment of Mallampatti grading.
- Measuring height and weight of the patient
- CVS,RS,and CNS examination of the patient.
- Spinal coloumn examination.

Investigations;

- Estimation of hemoglobin
- Bleeding time and clotting time

- Random blood sugar
- Blood urea and Serum creatinine.
- Standard 12-lead electrocardiogram

On the day of surgery, patients peripheral veins were cannulated with 18G IV cannulae, multipara monitors were attached like pulse rate, blood pressure, spo2 and ECG. 500 ml of RL was infused prior to procedure.

patients in sitting posture under strict aseptic precautions, epidural space was identified by loss of resistance technique to air and saline using 18G Tuohy needle via the midline approach at either L2-3 or L3-4 inter spinous space. An epidural catheter was inserted and fixed at 4 centimeters inside the epidural space. A test dose of 2 ml of 2% lignocaine with 1:200000 adrenaline was injected through the catheter after aspiration. After ruling out intrathecal and intravascular placement of the tip of the catheter, study drug was injected in incremental dose of 5 ml. The patients were changed from sitting to supine position after the procedure.

After the injection of 15ml of study drug which is taken as starting time, sensory and motor blockade were assessed at every minute the onset of sensory and motor block, the maximum level of sensory block, intensity of motor block and sedation score were noted. Using 22G needle Sensory blockade was assessed on the chest, trunk and lower limbs on each side.

Motor blockade was assessed by modified Bromage scale.

0 – able to lift the leg above from the bed for 5 seconds.

1– not able to lift the leg but able to flex the knee.

2 –not able to flex the knee but able to flex the ankle

3- not able to flex the ankle but able to move the toes

4 – not able to move the toes (total paralysis).

Table 1: Sedation scoring as per (Five point scale):

Alert and wide awake	1
Arousable to verbal command	2
Arousable with gentle tactile stimulation	3
Arousable with vigorous shaking	4
Unarousable	5

Measurements of blood pressure, heart rate, and oxygen saturation will be recorded every 5 minutes till the end of 1hour and then every 15 minutes till the end of surgery Intraoperatively and postoperatively complications like fall in blood pressure, variation in heart rate were noted, treated and tabulated.

Hypotension is defined as reduction of systolic blood pressure more than 30% from basal systolic blood pressure or SBP less than 90 mmHg and is treated with increased rate of intravenous fluids and if needed injection mephentermine 3 mg (I.V) given in increments. Bradycardia (<60 beats/min) was treated with injection Atropine 0.6 mg (I.V).

After the surgery, patients referred to the recovery room (PACU) post anaesthesia care unit where they remained until there was complete recovery of sensory and motor blockade. Epidural top up was given with 8ml of 0.2% inj. Ropicacaine once the patient complains of pain. Postoperatively vital parameters recorded every 15 minutes and also duration of sensory and motor blockade, any adverse events like nausea, vomiting, pruritis, shivering etc will be noted.

Onset of sensory blockade: is taken as the time from the completion of the injection of the study drug till loss of sensation at T10 level.

Onset of motor blockade: is taken from the completion of the injection of study drug till the patient develops modified Bromage scale grade 1 motor blockade.

Duration of motor block: is taken from the time of injection till the patient attains complete motor recovery (Bromage 0).

Duration of sensory block: is taken from the time of injection till the patient complains of pain at the T10 dermatome.

The results of the study were statistically analysed between the two groups.

STATISTICAL METHOD APPLIED

Statistical analysis was done using SPSS version 13.0. Descriptive statistics was done by calculating mean, standard deviation, range and proportion appropriately. The inferential statistics (test of significance) was done using unpaired t- test two way repeated measure ANOVA and chisquare test.

RESULTS

Table: 2 Showing age distribution

Age in yrs	Group R	Group RD
15-25	10	8
26-35	8	11
36-45	10	11
46-55	11	12
56-65	11	8
Total	50	50
Minimum Age in Yrs	20	18
Maximum Age in Yrs	60	56

Figure 6: Graph showing age distribution

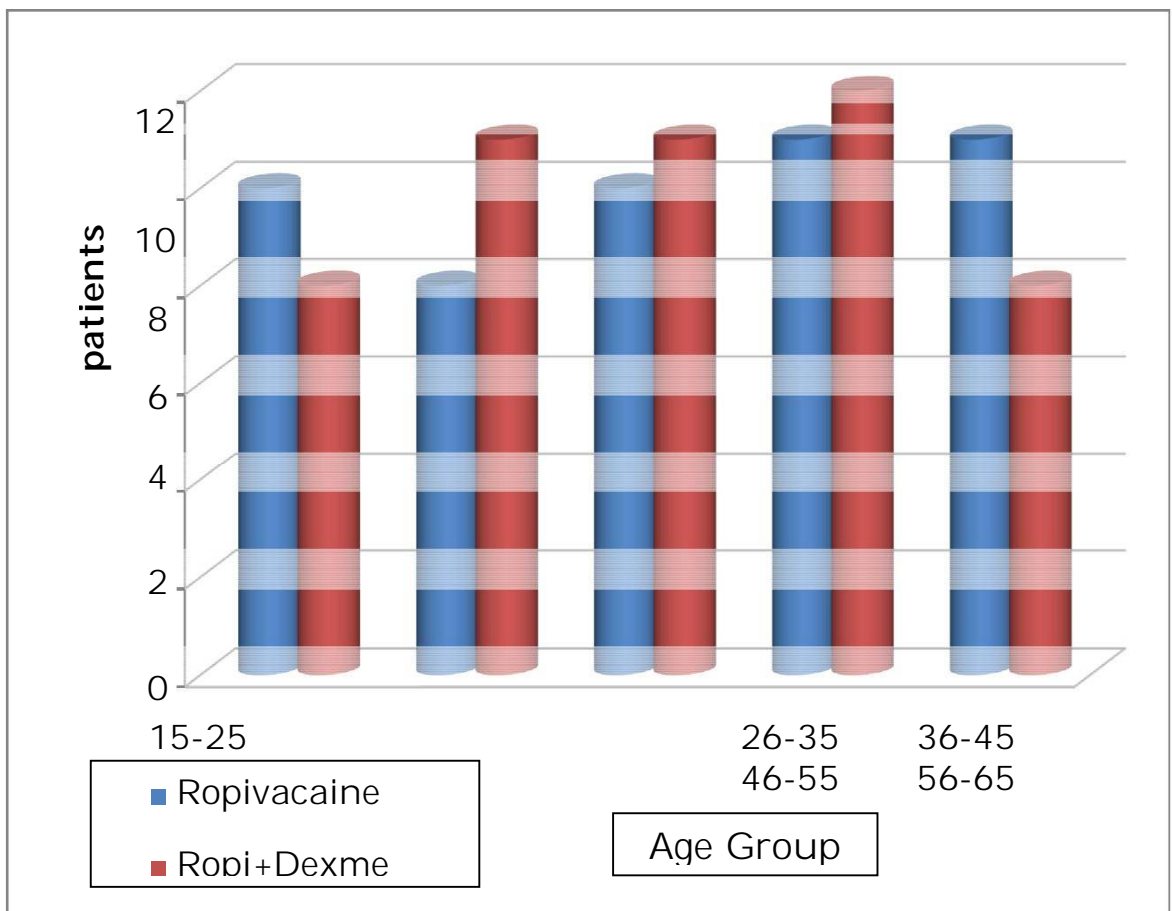


Table 2 and figure 6 showing age distribution of the patients in both the groups. The minimum age in groups R and RD were 18 and 20 years respectively. The maximum age in both groups R and RD was 65 years respectively. Age of the patient in both the groups were similar ($p>0.05$).

Table 3: Sex Distribution between Group R and Group RD

SEX	GROUP R		GROUP RD	
	No of patients	Percent	No of patients	Percent
MALE	36	72.0	31	62.0
FEMALE	14	28.0	19	38.0
TOTAL	50	100.0	50	100.0

Figure 7: Graph showing sex distribution

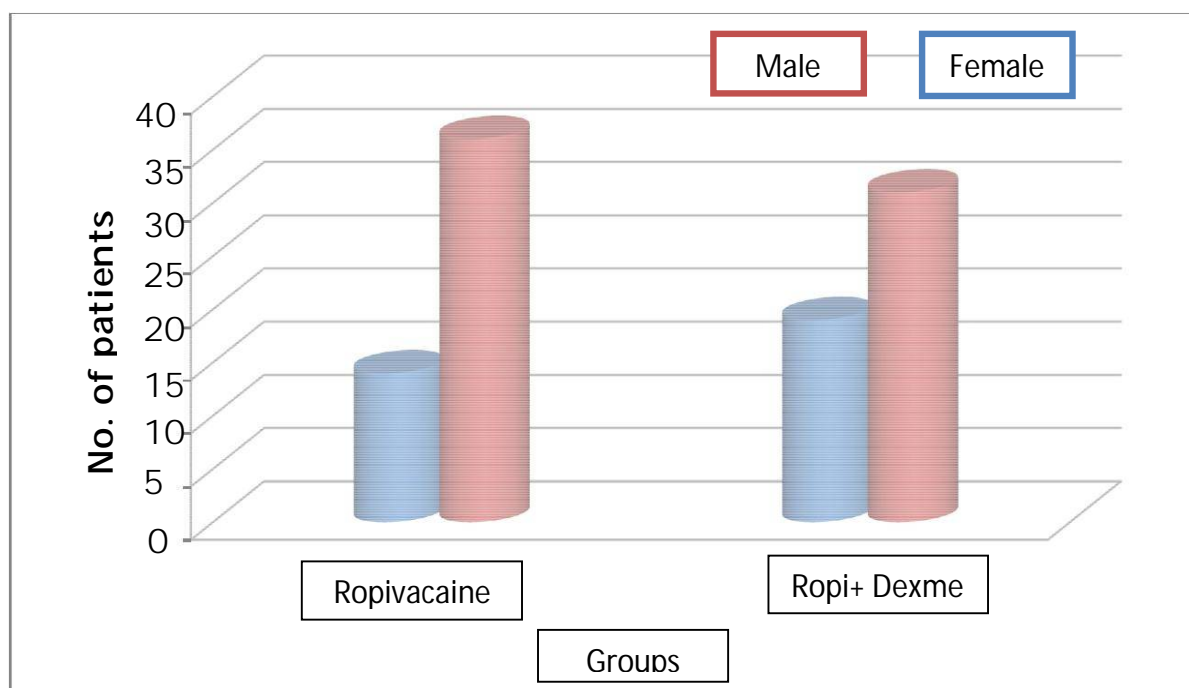


Table 3 and figure 7 showing the sex distribution of the patients in both the groups. There is no significant difference in the sex distribution of the patients between the groups. In both the groups there is a predominance of male patients.

Table 4: Showing the Body Weight distribution

	Group R	Group RD	p-value
Weight (in kgs)	58.64±5.17	56.10±6.11	0.27

Figure 8: Graph showing body weight distribution

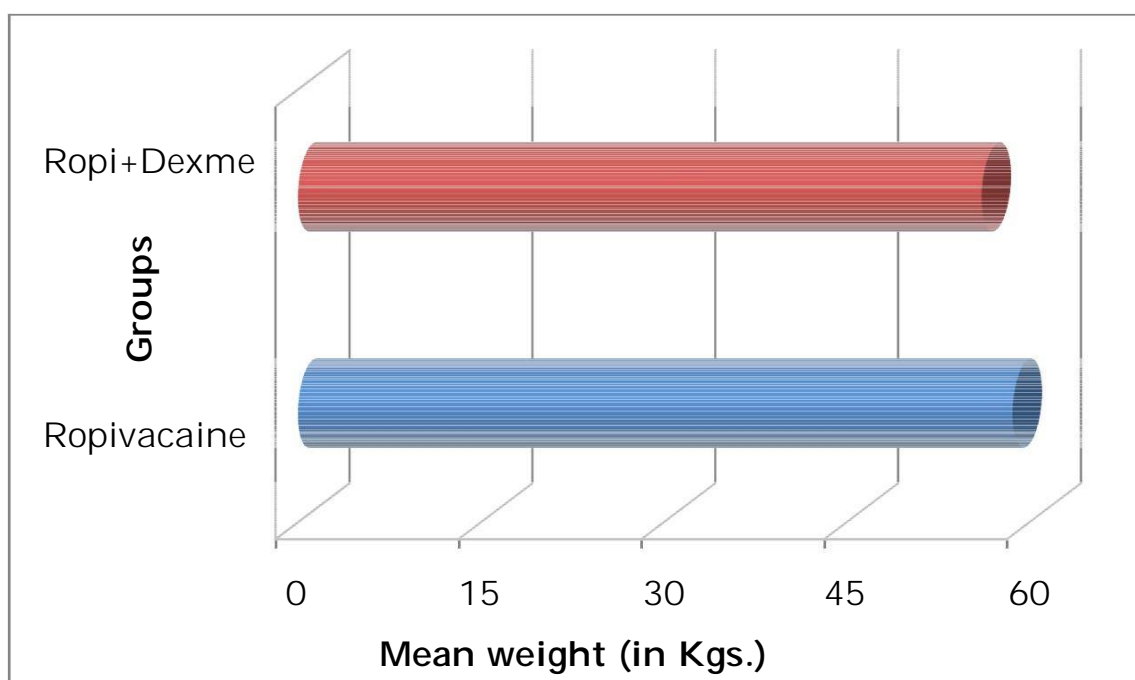


Table 4 and figure 8 showing the body weight distribution of patients. The mean body weight in group R is 58.64 ± 5.17 kg and group B is 56.10± 6.11 kg. No difference between two groups regarding the body weight (p=0.27).

Table 5: Height distribution

Height (cms)	Group R	Group RD
Mean height in cm	170	169.03
Minimum height in cm	150	152
Maximum height in cm	180	180

Figure 9: Graph showing body height distribution

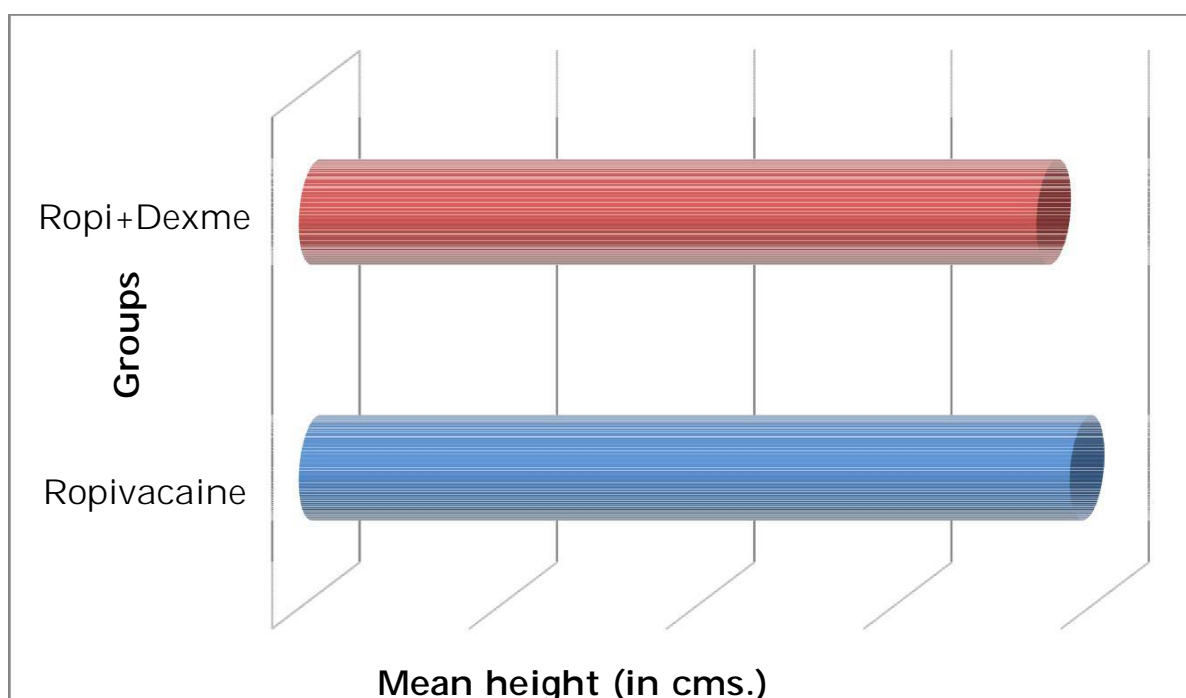


Table 5 and figure9 showing height distribution of patients. The mean height in group R is 170 centimeter and group RD is 169.03 centimeter. There is no difference between two groups regarding height.

Table 6: Type of surgical procedure

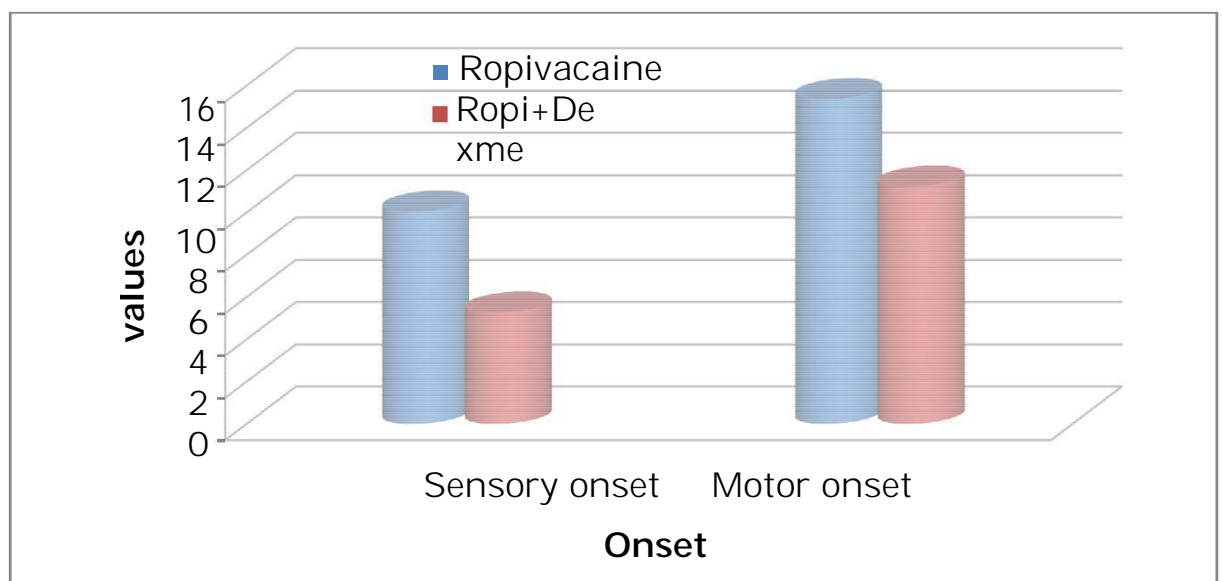
Type of surgery	Group R (Ropivacaine group)		Group RD (ropivacaine and dexmedetomidine group)	
	Number of Patients	Percent	Number of Patients	Percent
# Both bones leg	20	40	20	40
# Femur	30	60	30	60

There is no difference in the type of surgical procedures in both the groups

Table 7: Mean time for onset of sensory and motor block (minutes)

	Mean time for sensory onset (mins)	SD	p-value	Mean time for motor onset (mins)	SD	p value
Group R	10.04	2.55	0.00	15.36	3.28	0.00
Group RD	5.26	1.49		11.22	2.61	

Figure 11: Graph showing mean time for onset of sensory block (minutes)



The mean time of onset of sensory blockade in group R is 10.04 ± 2.5 mins and in group RD is 5.26 ± 1.49 mins. There is greater difference between two groups ($p=0.000$). The mean time for the onset of motor blockade is 15.36 ± 3.28 mins in group R and 11.22 ± 2.61 mins in group RD. There is greater difference between two groups ($p=0.000$).

Table 8: Maximum level of sensory blockade attained

Max Sensory level	Group R (No. of patients)	Group RD (No. of patients)	p-value
T5	0	5	0.10
T6	31	38	
T8	17	6	
T10	2	1	

Figure 12: Graph showing maximum level of sensory blockade attained

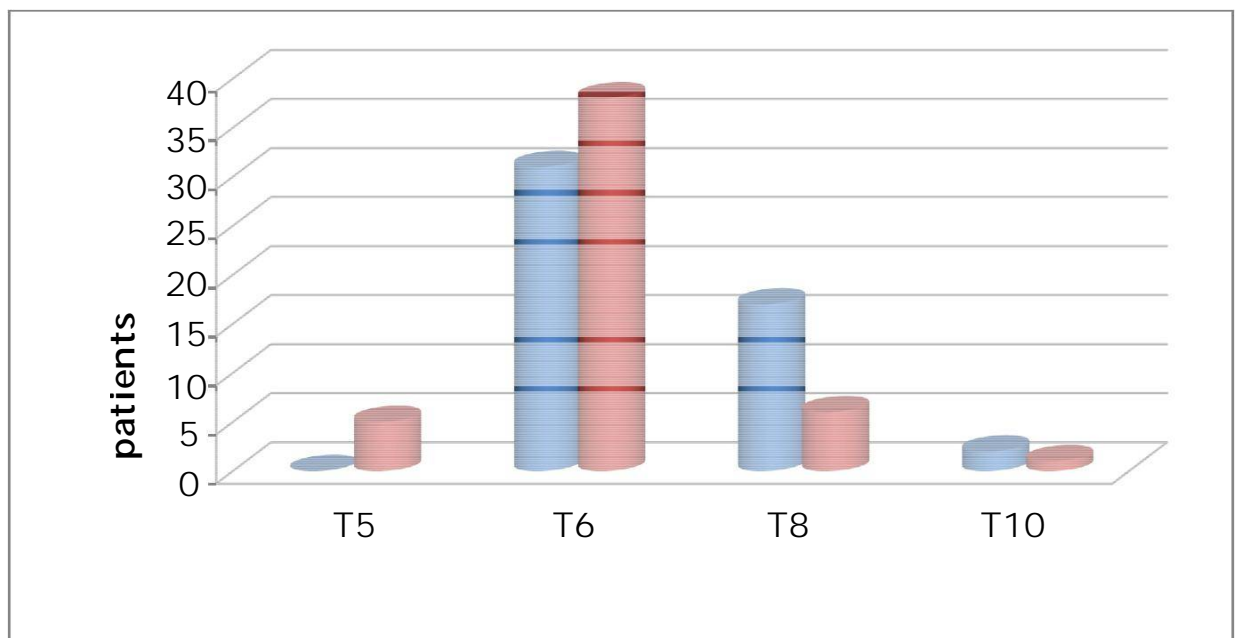


Table 8 and figure 12 showing maximum level of sensory blockade attained by the two groups. Group RD had the highest level of T5 and highest level in R group was T6. There is no difference between two groups ($p>0.05$)

Table 9: Grade of motor blockade

	Group R	Group RD	p-value
Bromage 2	15	0	<0.001
Bromage 3	35	34	0.35
Bromage 4	0	16	<0.001

Figure 13: Graph showing grade of motor blockade

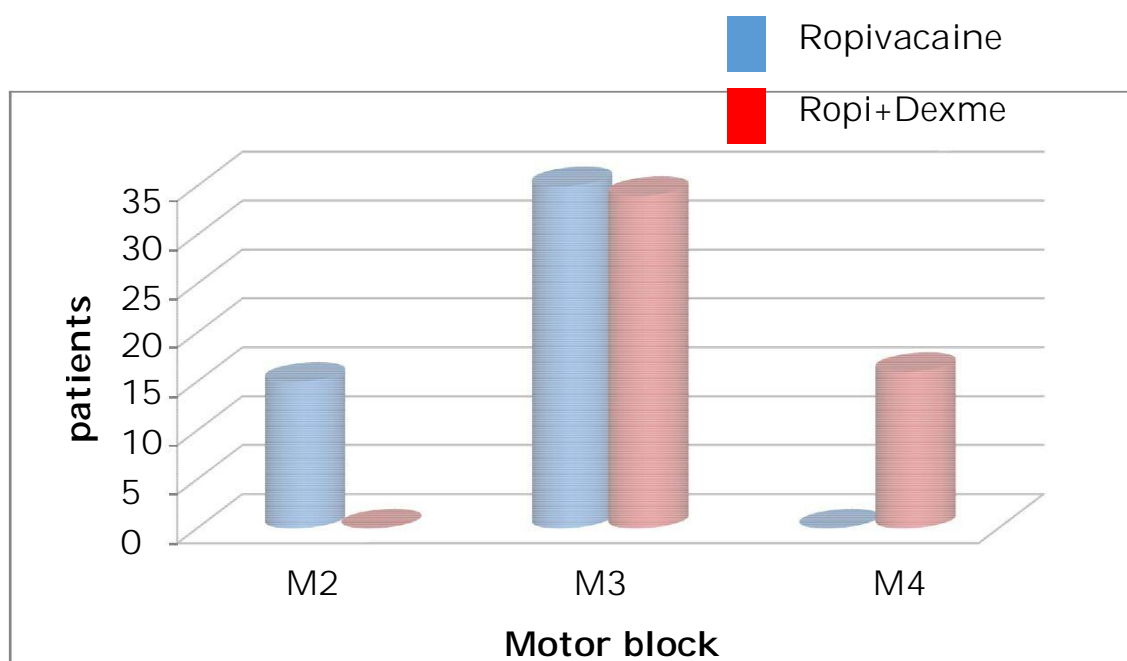


Table 9 and figure 13 showing grade of motor blockade in both the groups. 15 patients in group R had Bromage 2 and no patient in group RD, whereas patients with Bromage 4 were 0 in group R and 16 in group RD. More intense motor blockade of Bromage 4 was found in patients in group RD compared to patients in group R, the p value being 0.001 is highly significant.

Table 10: Sedation score

Sedation score	Group R	Group RD	p-value
S1	17	0	0.001
S2	33	15	
S3	0	29	
S4	0	6	

Figure 14: Graph showing sedation score

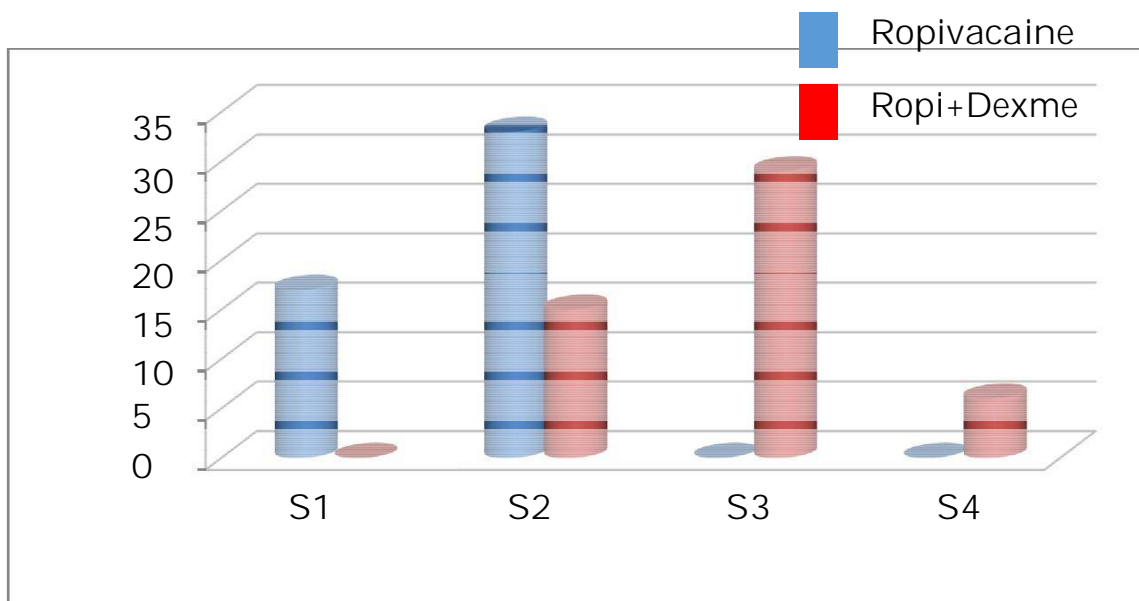


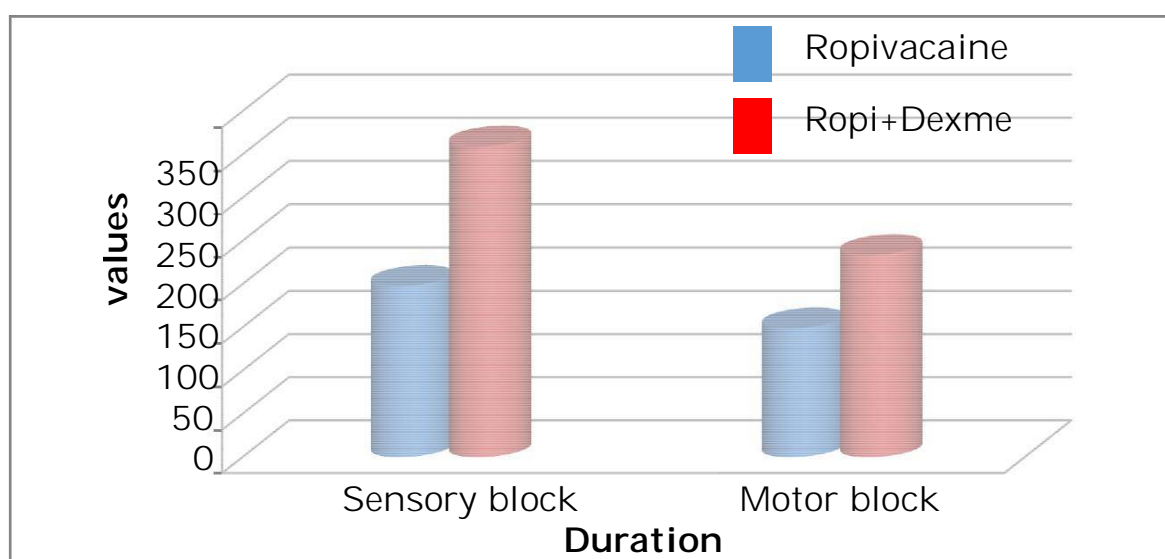
Table 10 and figure 14 showing sedation score in both groups.

Group R had the highest score of 2 and highest score in group RD was 4. Dexmedetomidine had greater scores compared to ropivacaine alone. ($p=0.001$).

Table 11: Duration of sensory and motor blockade (minutes)

	Mean	SD	p-value
Duration Of Sensory Block			
Group R	198.00	24.05	0.001
Group RD	359.30	61.94	
Duration Of Motor Block			
Group R	149.00	14.21	0.001
Group RD	233.70	15.36	

Figure 15: Graph showing Duration of sensory and motor blockade (minutes)

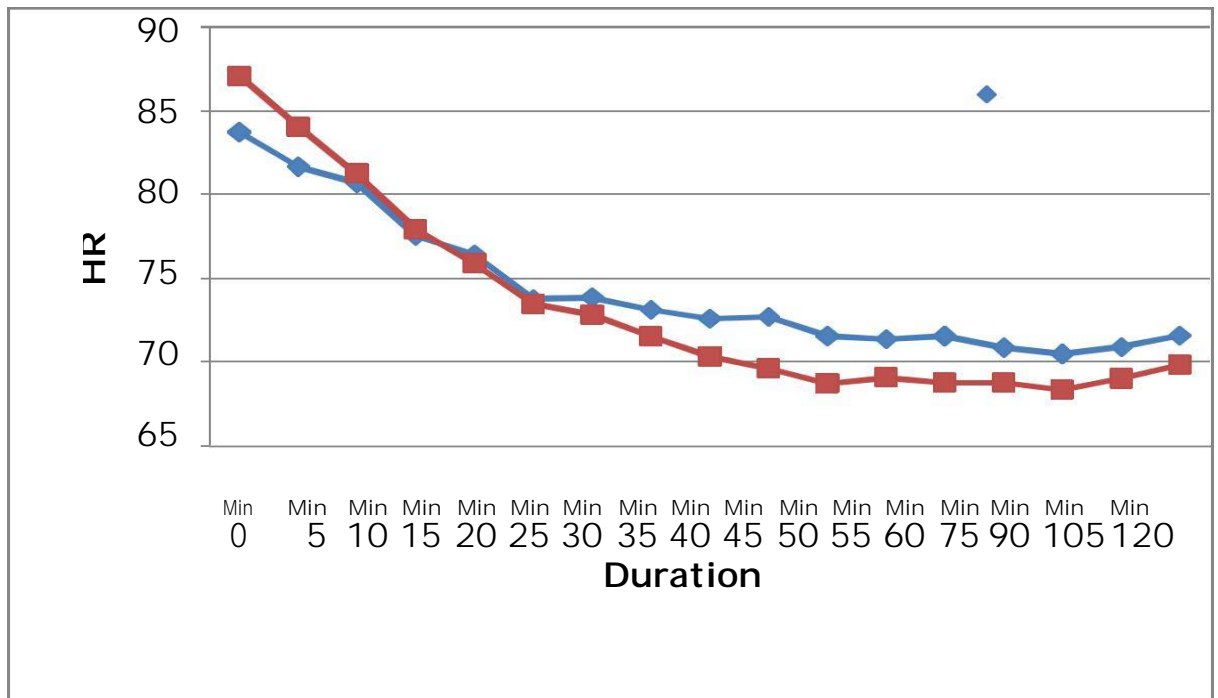


The mean duration of sensory block is 198.0 ± 24.05 minutes in group R and 359.30 ± 61.94 minutes in group RD. There is greater difference between two groups ($p=0.001$). The mean duration of motor blockade is 149.00 ± 14.21 mins in group R and 233.70 ± 15.26 mins in group RD. Statistically greater difference between two group ($p=0.001$)

Table-12: Mean heart rate (bpm) at various time intervals

	Group R	Group RD	p-value
HR-0min	83.72	87.06	0.62
HR-5min	81.68	84.04	
HR-10min	80.72	81.26	
HR-15min	77.54	77.92	
HR-20min	76.42	75.88	
HR-25min	73.78	73.46	
HR-30min	73.86	72.84	
HR-35min	73.14	71.54	
HR-40min	72.6	70.32	
HR-45min	72.7	69.6	
HR-50min	71.56	68.72	
HR-55min	71.38	69.08	
HR-60min	71.56	68.76	
HR-75min	70.86	68.76	
HR-90min	70.48	68.34	
HR-105min	70.9	69.02	
HR-120min	71.6	69.84	

Figure 16: Graph showing mean heart rate (bpm) at various time intervals

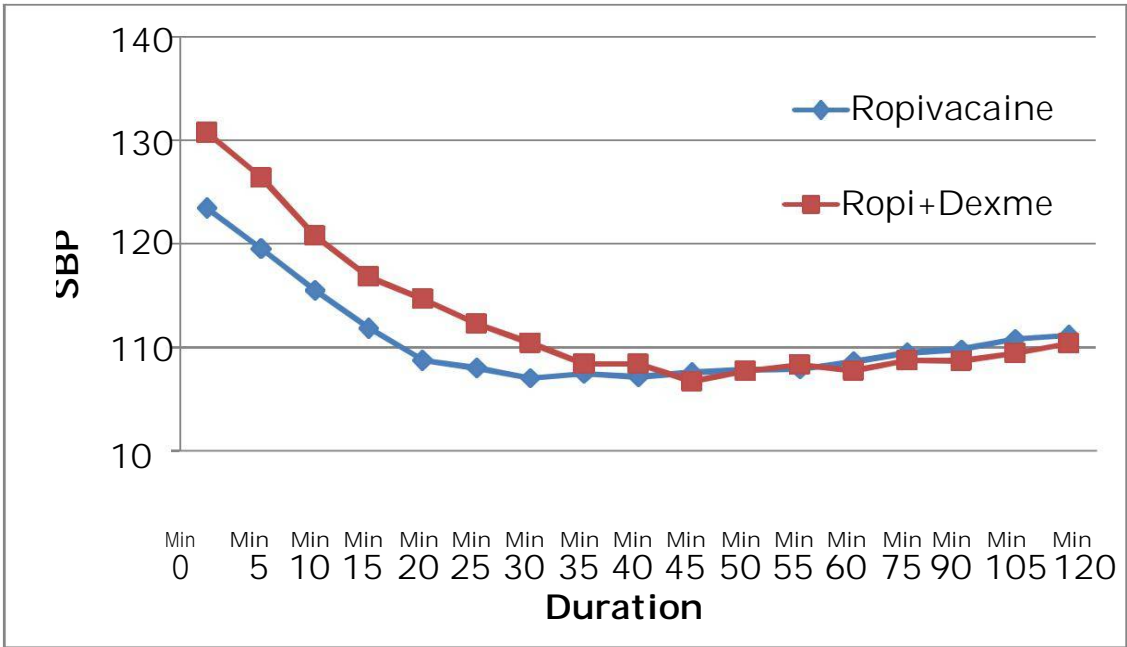


Significantly no difference in the mean heart rate between two groups.4 patients in RD group developed bradycardia which was treated with inj.atropine 0.6mg.

Table 13: Mean systolic blood pressure (mmHg) at various intervals

	Group R	Group RD	p-value
SBP-0min	123.42	130.74	0.8
SBP-5min	119.56	126.44	
SBP-10min	115.48	120.78	
SBP-15min	111.82	116.28	
SBP-20min	108.72	114.72	
SBP-25min	108.02	112.3	
SBP-30min	107	110.44	
SBP-35min	107.46	108.38	
SBP-40min	107.14	108.38	
SBP-45min	107.56	106.72	
SBP-50min	107.84	107.68	
SBP-55min	107.86	108.34	
SBP-60min	108.64	107.78	
SBP-75min	109.48	108.76	
SBP-90min	109.82	108.68	
SBP-105min	110.8	109.46	
SBP-120min	111.14	110.38	

Figure 17:Graph showing mean systolic blood pressure (mmHg) at various time intervals

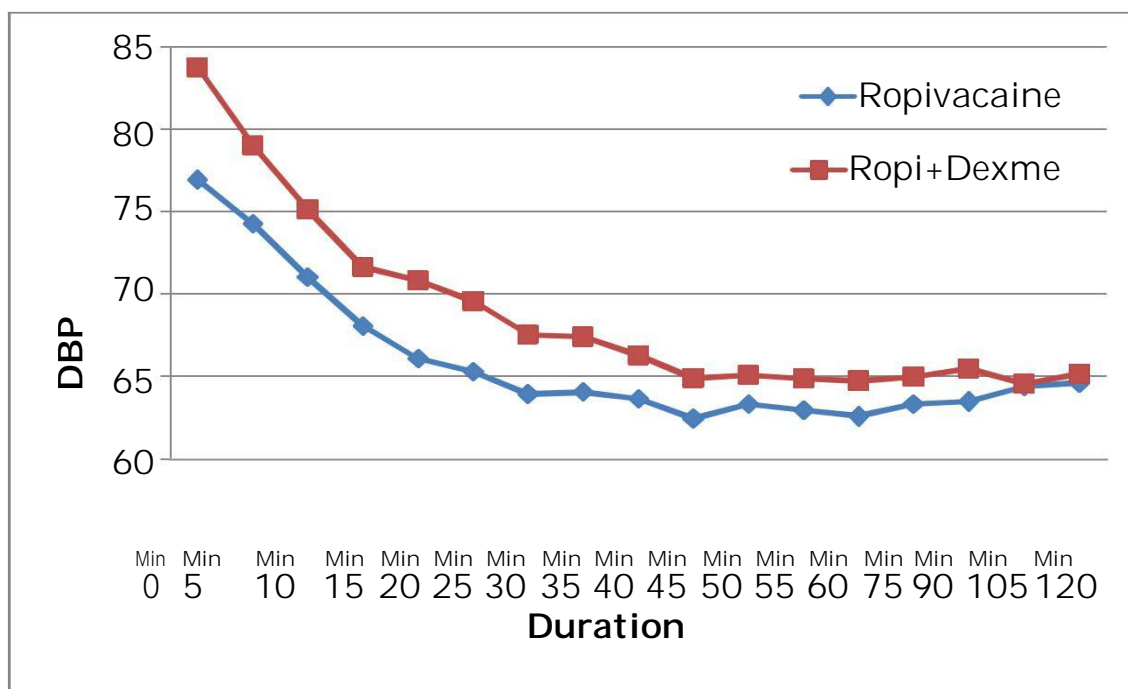


Significantly no difference in systolic blood pressure between two groups. 7 patients in group RD and 4 patients in group R developed hypotension which was treated with crystalloids and inj ephedrine.

Table14: Mean diastolic blood pressure (mmHg) at various time intervals

	Group R	Group RD	p-value
DBP -0min	76.94	83.76	0.4
DBP -5min	74.26	79	
DBP -10min	71.02	75.12	
DBP -15min	68.06	71.64	
DBP -20min	66.08	70.84	
DBP -25min	65.28	69.56	
DBP -30min	63.92	67.52	
DBP -35min	64.06	67.4	
DBP -40min	63.62	66.28	
DBP -45min	62.46	64.88	
DBP -50min	63.32	65.1	
DBP -55min	62.94	64.86	
DBP -60min	62.58	64.72	
DBP -75min	63.32	64.96	
DBP -90min	63.46	65.46	
DBP -105min	64.4	64.56	
DBP -120min	64.64	65.14	

Figure 18:Graph showing mean diastolic blood pressure (mmHg)at various time intervals

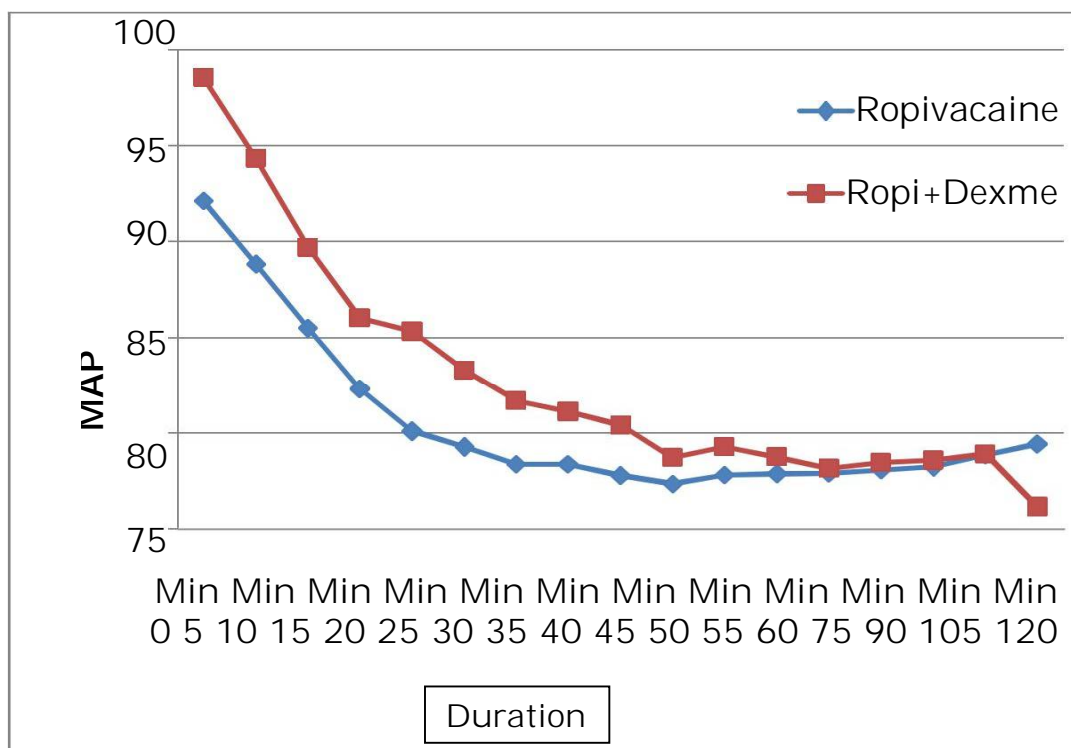


No much difference in diastolic blood pressure between two groups.

Table 15: Mean arterial pressure(mmHg) at various time intervals

	Group R	Group RD	p-value
MAP- 0min	92.12	98.58	0.5
MAP-5min	88.82	94.36	
MAP-10min	85.5	89.7	
MAP-15min	82.3	86.02	
MAP-20min	80.08	85.32	
MAP-25min	79.24	83.3	
MAP-30min	78.36	81.68	
MAP-35min	78.36	81.1	
MAP-40min	77.76	80.04	
MAP-45min	77.34	78.7	
MAP-50min	77.8	79.26	
MAP-55min	77.86	78.72	
MAP-60min	77.9	78.14	
MAP-75min	78.06	78.46	
MAP-90min	78.22	78.56	
MAP-105min	78.82	78.88	
MAP-120min	79.42	76.14	

Figure 19:Graph showing mean arterial pressure (mmHg) at various time intervals



No much difference in mean arterial pressure between two groups.

CONCLUSION

From the present study it can be concluded that

1. Regarding the onset of motor and sensory blockade both the groups shows clinically significant difference.
2. Ropivacaine and dexmedetomidine group produced more intense motor blockade than Ropivacaine group.
3. Duration of sensory block is prolonged with ropivacaine and dexmedetomidine group compared to Ropivacaine group.
4. Duration of motor block is also prolonged with ropivacaine and dexmedetomidine group compared to Ropivacaine group.
5. Ropivacaine and Dexmedetomidine group had higher sedation scores than ropivacaine group.
6. hypotension and bradycardia were not observed in any group.

Hence it can be concluded that dexmedetomidine given epidurally with ropivacaine produces synergistic effect of increase in duration of both motor and sensory blockade.

SUMMARY

A prospective randomized controlled study was undertaken to evaluate the sensory and motor blocking properties of epidurally administered 15 ml of Ropivacaine 0.75% and dexmedetomidine compared with Ropivacaine 0.75% in lower limb surgeries.

One hundred patients between the age group of 18-65 years belonging to ASA I and II posted for elective lower limb surgeries were randomly divided into two groups. Each group consisting of 50 patients to receive epidurally 15 ml of ropivacaine 0.75% (group R) and 15 ml ropivacaine 0.75% and dexmedetomidine 0.6 µg/kg (group RD).

Patients who had contraindications for epidural anaesthesia, patients posted for emergency surgery, height of the patient is less than 150 centimeter and more than 180 centimeter, pregnant patients and patients with BMI > 30 were excluded from the study.

In both the groups epidural space was identified in sitting position using loss of resistance technique and epidural catheter was introduced for 3 cms inside. After negative aspiration for blood and CSF, test dose with 3 ml of lignocaine 2% with adrenaline, 15 ml of the study drug was given in sitting position and the patient was put in supine position.

The onset, maximum level and duration of sensory and motor blockade and hemodynamic parameters were studied.

Table no 17: The following table shows the results obtained in the present study.

Group	Sensory onset (mins)	Motor onset (mins)	Max sensory level	Intensity of motor block	Duration sensory block (mins)	Duration of motor block (mins)	Sedation
R	10.04±2.5	15.36±3.2	T6	Br3	198±24	149±14.2	2
RD	5.26±1.4	11.2±2.6	T5	Br4	359.5±61	233±54.2	4

Dexmedetomidine group had rapid onset of action (p value of less than 0.001), sensory and motor blockade duration were prolonged (p value is less than 0.001), better sedation score (p=0.001), and determine more intense motor block (p<0.001). There was no difference in the maximal dermatomal level of analgesia, incidence of hypotension and bradycardia (p>0.05). The occurrence of side effects (tremor, nausea and SpO₂<90%) was low and similar between groups (p>0.05).

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PROFORMA

Patient name:	I.P.No:
Age:	Ward:
Sex:	Unit:
Address:	Date of admission:
	Date of sugery:
Diagnosis:	Operation:

Pre-anaesthetic evaluation

H/O:

Clinical examination:

Investigations

Pulse rate:	Hb%-
BP:	BT-
	CT-
Cardiovascular system:	Hiv/HbSAg/VDRL
Respiratory system:	FBS/PBS
Spine :	Blood urea
ASA GRADING :	Serum
Airway	creatinine
assessment: :	Blood group and
	Rh-
Weight:	ECG
Height:	CXR
BMI:	

Pre-Operative Instructions:

Anaesthetic management

Date:

Time:

Anaesthesia procedure:

Drugs used:

Onset of sensory block:

Onset of motor blockade:

Maximum dermatomal level of analgesia:

Intensity of motor blockade (Modified Bromage scale):

Sedation score (Five point scale):

Alert and wide awake	1
Arousable to verbal command	2
Arousable with gentle tactile stimulation	3
Arousable with vigorous shaking	4
Unarousable	5

Duration of sensory blockade:

Duration of motor blockade:

Vitals→ time in min ↓	PULSE RATE	SBP	DBP	MAP	SPO2
5					
10					
15					
20					
25					
30					
35					
40					
45					
50					
55					
60					
75					
90					
105					
120					
		98			



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Name of the Candidate : Dr. G.HEMA ALAMELU
Course : PG in MD., ANAESTHESIA
Period of Study : 2014-2017
College : MADURAI MEDICAL COLLEGE
Research Topic : COMPARATIVE STUDY OF EPIDURAL
0.75% ROPIVACAINE WITH
DEXMEDITOMIDINE AND 0.75%
ROPIVACAINE ALONE FOR LOWERLIMB
SURGERIES

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DISSERTATION SUBMITTED FOR
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BRANCH X (ANAESTHESIOLOGY)
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APRIL 2017

PAGE: 1 OF 100

21:40
26-09-2016

KEY TO MASTER CHART

cm	-	Centimeters
D	-	Dexmedetomidine
DBP	-	Diastolic blood pressure
F	-	Female
HR	-	Heart rate
I.P. No.	-	Inpatient number
Kg	-	Kilograms
ligno 2%	-	Inj Lignocaine 2% with adrenaline [1:200000]
m	-	Inj Mephentermine
M	-	Male
MAP	-	Mean arterial pressure
Mins	-	Minutes
mmHg	-	Millimeters of mercury
R	-	Ropivacaine
SBP	-	Systolic blood pressure
Sl.No.	-	Serial number
Wt.	-	Weight
#	-	Fracture

0.75% ROPIVACAINE ALONE

SL NO	IP NO	Age in yrs	Sex	weight (in kgs)	Type of surgery	Sensory onset(min)	Motor onset(min)	Max dermatomal level of analgesia	Intensity of motor block	Sedation	Duration of sensory block (min)	Duration of motor block (min)
1	19248	52	F	58	# BB LEG	8	13	T6	2	2	180	150
2	264623	50	F	60	#BBLEG	10	15	T6	3	2	180	150
3	20835	45	M	62	#IT femur	12	18	T8	3	2	210	135
4	20839	60	F	52	#IT femur	8	15	T8	2	2	210	150
5	20264	65	M	58	# BB LEG	16	21	T6	2	1	210	170
6	20420	32	M	58	#BB LEG	8	10	T8	2	2	270	210
7	20994	39	M	60	#BB LEG	8	13	T6	3	2	210	150
8	20995	60	F	51	#IT femur	12	18	T8	3	2	180	165
9	21002	40	M	63	# IT femur	12	15	T6	3	2	210	150
10	23438	55	F	52	# IT femur	10	18	T6	2	2	210	150
11	22578	32	M	60	# IT femur	8	12	T6	3	1	240	170
12	24051	38	M	70	#BB LEG	8	10	T10	3	1	210	150
13	24845	18	M	61	# BB LEG	10	15	T6	3	2	180	135
14	26043	51	M	74	# IT femur	8	12	T6	3	2	180	150
15	25321	65	F	58	# IT femur	12	18	T8	3	2	210	150
16	25890	50	M	59	# IT femur	15	18	T8	3	2	210	150
17	27788	60	M	58	# IT femur	8	15	T6	3	2	180	135
18	26128	60	F	52	# IT femur	8	10	T6	2	2	180	150
19	28540	60	M	60	# IT femur	8	12	T6	2	1	180	150
20	28949	24	M	62	# BB LEG	8	15	T6	2	1	210	150
21	1552	48	M	64	# BB LEG	10	18	T8	3	2	180	150
22	1285	30	M	58	# IT femur	12	18	T8	2	2	250	150
23	2246	58	M	60	# BB LEG	8	15	T6	3	2	180	135
24	2501	46	M	59	# IT femur	8	12	T10	2	1	180	150
25	2360	40	M	58	# BB LEG	8	12	T6	3	2	210	150
26	2472	25	M	60	# IT femur	10	18	T8	3	2	210	165
27	4223	40	M	62	# IT femur	8	15	T6	3	2	180	150
28	26047	60	M	60	# IT femur	12	15	T6	3	2	190	135
29	27459	62	F	50	# IT femur	12	15	T6	3	2	210	150
30	22096	25	F	52	#IT femur	10	12	T6	2	2	180	150
31	16288	21	F	51	# BB LEG	8	12	T6	3	2	180	135
32	16634	23	M	54	# BB LEG	13	15	T8	3	1	210	150
33	21983	65	M	58	# IT femur	15	18	T6	3	2	220	150
34	23693	43	M	61	# IT femur	20	25	T6	3	2	190	160
35	23141	24	M	64	# BB LEG	8	15	T8	3	2	135	105
36	25643	23	M	52	#BB LEG	8	12	T6	3	1	210	150
37	22944	48	M	60	# IT femur	10	18	T6	3	1	180	135
38	54095	29	M	61	# BB LEG	11	18	T6	2	1	210	150
39	11103	48	M	50	# IT femur	12	18	T8	3	1	180	150
40	14141	43	M	62	# IT femur	12	15	T6	3	2	210	160
41	13611	28	M	70	# IT femur	10	18	T8	2	2	180	150
42	69907	36	F	58	# IT femur	9	24	T6	3	1	220	150
43	50382	32	F	60	# BB LEG	8	15	T8	3	1	180	130
44	63821	24	M	65	#BB LEG	9	15	T8	3	2	210	135
45	64328	42	F	55	# IT femur	8	12	T8	3	1	190	150
46	949	25	F	50	# IT femur	10	12	T6	2	2	220	150
47	33484	32	M	56	# BB LEG	8	12	T6	2	2	210	165
48	721	29	M	59	# BB LEG	10	15	T6	3	1	220	150
49	33267	50	M	60	# IT femur	9	18	T6	3	1	180	135
50	589	55	M	55	# IT femur	9	18	T8	3	1	190	135

[illegible]

Ropivacaine with Dexmedetomidine																																		
IP NO	DBP0	DBP5	DBP10	DBP15	DBP20	DBP25	DBP30	DBP35	DBP40	DBP45	DBP50	DBP55	DBP60	DBP75	DBP90	DBP105	DBP120	MAP0	MAP5	MAP10	MAP15	MAP20	MAP25	MAP30	MAP35	MAP40	MAP45	MAP50	MAP55	MAP60	MAP75	MAP90	MAP105	MAP120
19248	74	74	65	73	69	61	62	74	60	52	47	45	56	58	60	69	76	90	87	79	83	83	76	75	81	70	64	59	56	66	67	68	69	76
264623	80	72	69	68	69	65	62	64	64	60	60	58	58	60	60	61	60	94	87	83	83	84	80	79	80	76	74	74	75	73	76	78	75	75
20835	80	78	78	76	76	75	76	72	72	70	72	70	68	65	69	69	66	89	87	88	88	84	83	81	81	78	79	78	81	77	74	74	75	75
20839	88	81	76	78	76	75	71	70	70	69	70	69	66	68	68	67	68	105	96	92	93	90	89	86	83	83	84	84	86	85	87	86	85	84
20264	78	63	51	51	53	60	56	52	51	49	52	52	52	60	61	60	62	92	75	57	57	60	70	65	62	62	58	68	67	68	69	69	68	68
20420	67	73	71	63	61	55	54	58	61	63	64	62	60	61	64	65	64	83	93	88	79	78	70	69	65	69	72	68	67	65	67	68	69	70
20994	75	68	73	63	52	58	50	62	77	63	66	69	71	71	66	78	68	89	79	88	74	69	72	76	76	83	75	78	78	82	80	81	80	82
20995	72	74	70	69	66	61	62	60	58	60	62	61	60	62	60	58	60	87	85	83	81	78	72	73	74	72	72	74	74	74	75	74	73	75
21002	70	66	67	65	62	60	57	58	56	58	60	60	58	55	56	58	55	90	86	85	82	80	80	76	77	78	80	80	79	78	75	75	76	76
23438	83	80	80	80	77	74	77	75	76	72	70	68	66	65	67	66	65	94	90	91	91	88	82	80	86	86	84	84	82	82	80	81	82	80
22578	74	75	67	67	65	64	62	65	65	63	65	61	61	62	60	62	62	91	90	83	80	80	80	78	80	80	79	80	80	76	78	75	76	74
24051	91	86	85	82	79	78	78	70	72	72	71	69	72	72	70	72	70	104	98	97	92	89	86	86	80	80	79	79	78	78	82	82	81	80
24845	82	80	78	70	69	68	67	68	69	66	65	64	64	67	66	64	64	100	94	92	87	85	85	86	86	83	84	80	80	81	81	83	80	80
26043	76	71	70	65	66	68	65	63	66	65	67	68	64	66	60	65	66	90	86	83	80	78	82	80	81	78	80	81	81	80	79	75	79	80
25321	70	72	65	64	65	60	61	56	55	56	57	54	51	56	55	52	54	81	81	75	73	73	70	69	66	67	68	67	67	65	67	68	67	68
25890	94	95	89	82	80	80	78	75	75	73	74	74	70	71	70	72	70	112	112	106	100	96	96	95	93	93	92	91	92	90	90	88	89	89
27788	80	80	69	68	65	67	67	66	67	68	62	70	72	68	68	65	66	94	93	80	81	80	81	81	82	82	83	80	83	83	82	82	80	80
26128	76	70	69	65	66	65	62	64	65	66	65	62	62	60	62	62	63	89	80	80	78	77	78	73	74	74	76	76	76	78	77	78	75	75
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1552	78	80	76	70	71	68	65	62	62	60	61	64	62	65	65	62	62	90	92	82	81	79	75	76	75	75	76	76	74	72	74	80	81	81
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2501	84	80	79	78	75	74	75	72	70	70	68	68	69	70	70	72	69	101	97	95	96	91	91	92	92	90	90	88	89	89	88	87	88	90
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4223	78	70	62	62	59	60	60	62	62	60	65	65	62	65	65	68	66	89	83	75	75	72	70	72	72	71	76	80	78	78	80	78	82	84
26047	81	80	79	74	71	70	68	65	65	67	68	68	69	70	71	70	72	97	95	93	90	91	89	85	87	85	86	84	85	85	82	80	81	80
27459	86	85	80	79	73	72	74	70	72	71	74	74	72	70	69	69	70	97	92	91	91	86	84	85	83	84	84	85	87	87	85	85	86	86
22096	80	82	82	76	75	76	72	70	72	70	70	72	70	68	65	68	68	94	94	93	90	89	90	88	84	88	89	89	88	88	87	86	89	88
16288	66	65	58	71	71	68	62	67	70	55	60	64	64	70	60	70	68	83	81	84	87	85	87	79	85	88	75	80	87	84	85	82	88	88
16634	62	58	51	49	59	57	57	48	49	50	50	50	50	51	52	50	51	77	77	70	73	76	76	76	72	72	73	75	73	73	74	72	68	64
21983	84	73	53	50	45	57	57	68	61	65	74	69	66	63	69	68	79	106	95	68	63	56	71	70	87	80	82	86	87	85	84	86	89	96
23693	74	71	79	75	76	78	77	77	74	76	75	72	70	72	71	72	74	89	84	90	87	86	88	89	89	88	87	88	86	84	88	89	87	89
23141	80	79	76	75	78	78	76	77	79	77	75	74	76	75	72	74	75	95	92	93	90	92	91	94	94	96	98	95	90	92	90	89	89	90
25643	75	75	71	68	65	63	61	62	59	62	65	62	64	65	62	65	65	83	86	82	81	77	74	71	71	68	70	69	70	74	75	76	75	74
22944	98	94	89	63	54	58	57	64	53	65	64	67	65	65	71	76	76	128	127	115	79	72	73	70	75	63	79	79	78	84	79	84	91	97
54095	71	75	71	71	69	65	66	74	64	65	67	65	66	64	64	65	65	93	97	93	93	93	90	88	92	93	87	87	90	87	86	85	85	85
11103	80	76	70	68	68	65	62	60	62	60	64	60	62	64	60	60	58	97	94	87	85	84	82	79	77	78	78	80	79	79	80	79	79	75
14141	60	58	55	53	52	50	50	48	49	50	52	50	51	50	54	52	52	77	75	72	68	67	64	65	64	65	67	68	69	68	67	61	70	70
13611	68	62	64	60	59	58	55	56	55	56	57	55	50	54	55	53	57	87	80	82	77	75	76	74	72	70	74	74	73	67	68	69	70	74
69907	72	69	67	63	61	57	54	57	56	42	42	50	45	50	69	73	73	90	85	84	81	78	69	76	75	73	56	57	68	71	72	90	94	98
50382	80	80	78	70	70	69	70	68	65	64	66	67	68	64	68	68	68	94	92	89	83	83	81	82	79	78	78	83	81	81	80	82	80	80
63821	70	66	65	67	67	62	61	62	59	58	58	60	61	60	62	60	59	85	80	78	80	79	76	75	76	75	72	75	77	76	77	78	76	75
64328	68	68	62	69	58	59	56	55	56	57	57	58	60	60	58	58	60	86	85	81	85	76	75	73	70	71	71	72	72	73	73	75	75	76
949	70	64	64	59	56	56	55	50	50	49	52	52	54	53	54	54	56	80	76	76	72	69	69	67	63	63	63	66	66	67	68	66	66	68
33484	72	68	68	69	66	65	65	62	64	60	59	60	62	62	60	62	62	91	85	86	85	83	81	81	79	81	76							

					Ropivacaine with Dexmedetomidine							
SL NO	IP NO	Age in yrs		Weight (in kgs)	Type of surgery	Sensory onset(min)	Motor onset(min)	Max dermatomal level of analgsia	Intensity of motor block	Sedation score	Duration of sensory block(min)	Duration of motor block(min)
1	16266	38		54	# IT femur	8	12	T6	4	3	255	240
2	19079	45		50	# IT femur	4	6	T6	3	3	320	280
3	19246	48		50	# IT femur	9	15	T6	3	3	300	210
4	19578	45		55	# BB LEG	4	5	T6	4	2	300	220
5	19967	21		61	# IT femur	4	5	T6	3	2	435	280
6	20405	50		50	# BB LEG	4	8	T6	3	3	400	270
7	21571	50		50	# BB LEG	4	6	T6	3	3	330	240
8	21700	60		55	#BB LEG	4	9	T6	4	3	330	210
9	23084	65		65	#BB LEG	5	10	T6	3	3	390	300
10	23102	61		50	#IT femur	6	12	T6	3	2	450	330
11	23870	50		50	# IT femur	5	9	T6	3	2	360	210
12	24035	38		65	# IT femur	6	15	T6	3	2	260	210
13	24220	40		70	#BB LEG	4	11	T6	4	2	320	180
14	24842	60		65	#IT femur	4	11	T8	3	3	350	210
15	25375	58		62	# IT femur	5	11	T6	3	3	400	270
16	25958	52		50	# BB LEG	4	12	T6	3	4	350	210
17	25410	52		54	# IT femur	4	6	T6	3	3	390	330
18	26955	58		50	# BB LEG	6	11	T8	4	3	400	270
19	372540	35		53	# IT femur	5	11	T6	3	3	310	190
20	29010	27		58	# BB LEG	4	10	T6	3	3	360	180
21	462	52		50	# IT femur	4	12	T6	4	4	310	190
22	822	45		50	# BB LEG	5	12	T6	4	4	390	210
23	1413	28		64	# IT femur	3	11	T5	3	3	390	210
24	2107	36		60	# BB LEG	6	10	T6	3	4	390	230
25	1853	28		52	# IT femur	5	15	T8	3	3	400	280
26	1913	20		50	# IT femur	7	15	T6	4	3	360	180
27	1031`	28		55	# BB LEG	7	15	T6	4	2	310	190
28	2874	21		61	# IT femur	6	12	T6	3	3	310	210
29	3429	26		50	# IT femur	4	10	T6	3	3	390	210
30	24517	55		62	# IT femur	3	10	T6	3	3	540	405
31	25645	54		50	# BB LEG	6	13	T6	3	2	400	270
32	23432	43		60	# IT femur	4	12	T5	4	2	480	330
33	11098	48		50	# BB LEG	5	12	T6	3	3	340	210
34	11209	23		70	# BB LEG	7	15	T6	3	4	480	320
35	12334	24		50	# IT femur	8	12	T10	3	2	510	380
36	1207	22		50	# BB LEG	4	15	T6	3	2	280	170
37	1230	30		54	# IT femur	5	12	T6	3	2	310	190
38	1412	42		52	# IT femur	7	14	T8	4	3	375	210
39	1902	50		60	# BB LEG	6	11	T6	3	2	360	210
40	2314	28		58	# IT femur	7	12	T6	4	2	390	210
41	2436	20		59	#IT femur	7	12	T6	4	2	310	240
42	2891	48		64	# IT femur	9	11	T6	4	3	300	210
43	3217	34		54	# IT femur	4	10	T5	3	3	310	180
44	3462	56		54	# IT femur	4	12	T5	3	3	360	210
45	5769	62		50	# BB LEG	4	10	T8	4	3	390	240
46	4721	40		53	# IT femur	6	10	T6	3	4	310	190
47	4734	42		62	#IT femur	4	10	T6	3	3	280	180
48	5102	28		56	#IT femur	5	12	T6	3	3	360	180
49	7906	25		68	#BB LEG	7	15	T8	4	3	310	190
50	7388	22		60	#BB LEG	5	14	T5	3	3	310	210

	ropivacaine with dexmedetomidine																																	
	HR-0	HR5	HR10	HR15	HR20	HR25	HR30	HR35	HR40	HR45	HR50	HR55	HR60	HR75	HR90	HR105	HR120	SBP0	SBP5	SBP10	SBP15	SBP20	SBP25	SBP30	SBP35	SBP40	SBP45	SBP50	SBP55	SBP60	SBP75	SBP90	SBP105	SBP120
16266	116	110	110	103	103	89	93	95	89	86	85	84	89	89	92	95	95	138	132	128	124	127	109	114	113	110	97	102	102	100	104	108	108	108
19079	109	116	120	113	96	88	90	90	86	87	89	96	94	93	90	86	81	143	141	134	122	108	106	110	108	108	104	101	100	89	110	111	103	99
19246	92	94	90	86	94	80	70	77	70	73	67	64	65	64	68	70	80	130	127	124	118	125	117	120	109	108	106	98	92	101	98	98	102	109
19578	87	78	76	67	66	67	70	69	70	66	71	76	76	75	66	65	68	114	80	102	100	95	95	98	90	93	90	109	117	113	107	105	107	110
19967	75	67	59	57	55	58	57	57	56	62	58	57	59	56	56	60	62	117	114	116	100	111	107	103	100	107	104	94	102	108	116	114	117	118
20405	84	79	74	76	71	68	70	73	72	66	68	65	66	65	65	64	67	146	148	142	138	138	130	128	132	128	120	122	120	118	124	120	120	124
21571	74	70	65	61	60	61	61	60	60	61	60	60	59	60	73	75	75	110	118	107	109	97	94	98	95	98	96	94	98	115	110	108	110	110
21700	78	70	71	66	62	59	72	71	73	74	74	72	71	70	72	70	72	145	129	113	93	111	107	96	118	113	115	97	103	105	108	108	105	106
23084	65	60	54	56	50	53	53	50	50	51	50	50	51	51	56	54	56	140	146	136	113	116	117	112	112	114	114	115	117	117	126	131	134	134
23102	68	65	68	72	70	65	64	61	58	56	55	55	55	54	54	65	65	148	140	156	161	139	131	128	120	115	110	115	122	118	120	127	119	120
23870	80	76	77	78	72	71	70	72	70	69	68	69	66	65	65	67	65	124	118	112	116	112	110	102	102	100	98	102	102	100	106	105	106	106
24035	82	80	76	76	72	68	68	70	78	76	77	78	74	76	82	82	83	153	146	134	138	144	148	140	133	133	133	133	135	139	140	136	137	136
24220	86	84	84	80	80	79	74	70	68	70	76	78	91	92	88	86	88	129	117	104	99	103	94	104	99	100	103	103	103	103	104	102	98	102
24842	90	80	69	58	56	57	57	56	55	56	55	55	55	63	63	64	64	133	108	96	90	92	92	94	94	89	89	109	106	103	106	108	108	108
25375	84	84	82	80	78	79	80	76	74	70	71	69	68	68	67	65	66	150	144	126	118	120	108	102	98	114	112	108	104	107	108	110	108	110
25958	78	70	72	72	71	70	68	69	68	67	66	67	65	64	65	62	62	114	98	90	102	106	104	110	108	106	102	98	110	108	108	106	110	112
25410	76	75	78	72	70	68	65	62	60	57	58	54	55	56	56	55	57	122	110	112	110	98	96	96	90	92	92	108	106	106	102	108	110	108
26955	98	95	90	86	82	80	74	75	70	68	65	64	66	65	67	67	68	146	146	140	132	118	120	118	116	112	116	118	120	118	122	120	126	126
372540	80	80	76	77	73	72	74	71	69	68	68	69	70	72	71	70	71	110	104	97	94	90	89	89	90	89	104	102	104	104	106	106	102	102
29010	102	100	98	94	95	93	90	91	90	88	85	86	82	78	76	75	72	138	140	145	140	130	130	128	120	122	120	124	120	118	120	121	124	120
462	98	99	89	96	86	89	88	88	84	83	81	82	75	73	68	74	72	158	144	110	102	90	130	112	128	105	103	104	96	86	88	90	102	99
822	99	96	95	93	97	91	93	93	91	88	88	88	88	87	88	87	86	110	101	104	103	103	98	99	96	92	89	94	89	91	93	97	97	98
1413	125	126	113	111	104	98	101	102	98	98	97	105	103	110	96	98	94	107	104	89	96	108	108	105	99	97	96	94	106	103	110	96	102	108
2107	86	80	76	75	76	70	71	75	74	77	76	75	74	75	70	72	73	124	126	122	120	118	116	115	110	112	110	114	112	116	115	112	114	116
1853	96	92	90	76	82	82	76	74	77	76	74	68	68	65	64	64	66	159	151	129	120	128	133	130	130	118	120	118	120	120	110	97	110	110
1913	103	106	90	73	69	64	62	54	53	52	53	64	60	55	50	60	76	130	131	128	120	123	121	114	117	111	108	128	131	120	108	104	112	128
1031	101	95	90	92	85	82	80	76	72	70	68	69	70	68	66	67	68	122	120	112	108	106	110	108	105	104	102	105	108	110	106	108	110	112
2874	70	69	70	66	65	61	60	56	59	59	56	55	54	54	55	54	54	136	138	130	126	126	121	120	112	110	110	112	110	108	109	108	110	109
3429	79	75	76	75	72	71	71	70	69	65	64	67	67	65	65	64	64	128	110	102	100	96	103	104	98	95	95	98	98	96	95	98	102	98
24517	85	83	71	79	69	70	69	65	65	63	59	59	61	58	60	61	64	144	136	127	136	122	120	121	118	114	115	107	101	110	112	108	106	106
25645	121	124	118	80	85	81	79	79	81	82	81	80	80	80	84	77	76	126	112	100	98	103	106	95	98	114	94	104	102	96	95	101	94	110
23432	94	90	82	80	84	80	79	76	79	76	75	75	74	74	71	70	72	118	109	108	107	100	92	85	82	102	98	92	95	97	92	92	94	94
11098	91	89	89	87	85	82	82	83	80	80	76	78	75	72	71	73	72	126	135	136	131	128	121	114	109	110	116	112	110	108	109	108	110	110
11209	88	85	88	86	85	85	84	84	85	82	78	75	75	76	75	80	82	130	128	130	134	130	128	128	128	130	128	126	120	118	118	118	120	120
12334	70	68	68	65	64	64	64	65	64	62	64	60	59	63	64	59	58	130	134	130	128	126	126	124	120	120	120	118	124	118	120	118	112	112
1207	68	65	65	69	63	65	63	63	60	59	58	56	60	62	60	62	60	138	140	146	135	129	124	125	121	121	114	104	100	112	112	114	110	108
1230	82	83	80	81	82	80	79	77	77	75	74	75	75	76	74	74	75	120	128	130	124	116	114	107	108	110	108	112	112	109	109	110	108	109
1412	95	96	95	92	92	90	90	89	85	87	85	82	81	84	82	82	82	134	140	136	126	132	130	128	125	128	126	126	124	118	120	118	119	116
1902	71	70	72	70	69	69	67	68	69	68	68	67	65	65	63	65	65	118	116	116	112	112	104	106	98	100	99	102	102	103	102	104	104	102
2314	87	86	85	83	83	80	79	78	79	76	76	75	77	74	73	74	74	122	135	134	126	120	108	108	106	104	108	108	110	110	108	112	110	109
2436	104	100	102	101	99	96	95	90	89	88	86	89	88	90	89	88	89	154	165	132	130	132	118	118	120	124	122	120	124	120	118	119	118	118
2891	84	86	82	81	78	77	79	76	76	75	77	78	77	76	78	78	78	142	146	140	138	140	136	132	130	132	128	130	129	128	128	126	132	130
3217	80	79	80	78	77	75	76	70	66	65	60	59	58	58	59	58	60	140	144	138	130	128	122	120	122	120	116	118	122	122	125	124	120	120
3462	68	67	62	62	60	59	56	52	51	52	52	51	50	50	52	51	52	144	134	132	130	122	112	110	116	118	114	110	108	104	102	104	110	108
5769	78	75	72	70	70	66	64	62	55																									

Ropivacaine with Dexmedetomidine																																		
IP NO	DBP0	DBP5	DBP10	DBP15	DBP20	DBP25	DBP30	DBP35	DBP40	DBP45	DBP50	DBP55	DBP60	DBP75	DBP90	DBP105	DBP120	MAP0	MAP5	MAP10	MAP15	MAP20	MAP25	MAP30	MAP35	MAP40	MAP45	MAP50	MAP55	MAP60	MAP75	MAP90	MAP105	MAP120
16266	90	80	90	80	80	79	73	76	73	70	70	72	67	70	72	72	70	102	100	98	97	95	86	88	90	88	72	77	78	82	80	81	79	80
19079	104	85	56	66	54	62	45	45	49	45	45	45	47	54	50	53	56	101	95	80	80	75	64	72	62	60	61	55	54	54	65	58	70	66
19246	70	68	66	65	68	69	68	65	62	60	58	55	56	56	56	57	58	90	87	85	82	84	82	84	81	82	82	78	76	74	76	75	76	74
19578	78	62	68	65	65	64	63	60	62	60	64	67	67	65	65	66	65	90	68	81	76	75	74	74	70	72	70	79	82	81	80	80	79	79
19967	75	76	72	64	63	63	63	69	67	61	64	64	61	70	65	65	67	93	91	91	78	77	87	82	84	79	84	83	77	84	85	88	85	88
20405	90	92	90	87	85	81	80	80	79	76	77	75	75	76	72	71	72	108	110	107	104	103	100	99	99	96	90	91	89	85	88	88	88	88
21571	80	76	72	52	68	62	56	61	50	61	61	61	52	57	83	65	65	89	86	84	67	83	74	71	77	64	77	74	74	72	70	90	73	75
21700	92	76	65	57	66	62	51	69	64	63	54	50	62	60	62	60	60	103	86	76	66	75	72	60	85	76	74	65	64	71	71	69	72	72
23084	79	81	79	66	65	63	65	66	71	68	71	68	68	76	78	76	78	93	96	93	78	77	76	76	77	82	79	82	81	79	89	92	89	92
23102	88	87	87	82	75	72	72	68	69	65	66	68	68	68	70	71	69	108	104	110	108	96	91	90	85	83	80	81	86	85	85	87	85	85
23870	76	69	68	70	65	64	60	60	62	60	64	64	60	62	64	64	64	92	85	82	85	80	79	76	77	75	73	74	75	73	75	75	76	76
24035	92	85	81	82	90	95	92	82	79	76	82	80	84	82	80	76	84	106	99	92	95	104	108	104	95	93	90	94	92	96	94	92	90	92
24220	89	67	61	55	60	55	56	59	58	58	57	58	54	59	59	58	58	98	79	71	65	70	65	66	67	68	68	69	68	65	71	68	70	68
24842	75	65	56	59	60	61	61	60	61	60	59	71	71	71	68	68	70	97	81	69	70	70	71	72	73	72	69	69	85	83	82	80	80	82
25375	96	92	84	81	80	78	78	72	70	70	69	70	68	68	69	70	70	114	109	96	93	93	88	86	80	84	84	82	81	82	81	84	84	83
25958	70	64	60	60	58	60	61	62	62	60	58	60	60	62	62	60	65	84	75	70	74	74	74	74	74	75	72	72	75	76	76	74	76	76
25410	80	72	75	67	61	60	55	56	55	55	58	58	58	54	56	58	58	93	85	82	74	72	68	67	67	74	74	72	72	74	72	72	74	74
26955	96	102	100	90	82	84	84	80	78	75	76	76	78	74	74	75	75	112	116	112	104	94	96	94	92	90	90	91	92	90	90	92	94	92
372540	70	66	60	54	56	52	50	49	49	50	52	52	50	50	56	54	54	83	78	72	67	67	64	63	68	69	68	72	70	68	68	70	72	70
29010	90	92	92	88	87	85	80	81	80	76	78	75	72	71	71	70	70	106	108	108	101	99	96	96	97	94	93	94	90	89	89	88	89	84
462	105	95	70	71	70	87	78	77	67	66	71	66	57	56	49	69	65	127	110	87	83	78	105	90	91	83	81	83	78	69	68	61	83	80
822	75	51	58	60	57	64	60	59	58	56	58	55	53	57	59	61	60	87	75	77	75	74	76	77	72	72	70	74	71	63	71	74	77	77
1413	71	62	45	63	68	65	62	61	56	45	50	57	52	53	57	57	56	80	77	61	76	84	80	79	76	71	62	73	70	69	66	73	73	71
2107	82	80	79	76	70	69	70	65	65	65	67	66	67	62	60	61	60	96	95	93	90	87	84	85	82	82	80	82	80	80	82	82	80	80
1853	108	104	85	85	90	90	86	86	78	80	80	80	76	80	76	58	58	122	120	99	97	101	102	100	100	92	92	91	92	84	86	81	83	83
1913	82	82	79	76	76	72	70	70	68	72	70	72	68	65	65	64	65	98	98	92	90	90	88	85	85	82	85	92	90	89	80	78	60	84
1031	78	75	70	69	70	65	66	67	67	64	64	65	67	67	66	67	67	92	90	84	82	82	78	78	76	79	76	76	77	79	79	75	77	76
2874	102	102	98	95	88	85	86	88	85	82	82	80	80	78	78	80	80	113	114	108	105	100	97	95	95	95	92	92	90	88	86	85	90	89
3429	70	65	61	56	56	57	56	58	55	56	58	58	60	56	57	56	58	89	80	74	70	69	72	72	70	67	67	68	68	70	68	68	71	72
24517	84	82	75	82	73	71	74	72	68	67	57	58	59	57	59	57	59	106	100	92	100	92	90	90	89	87	86	85	78	75	75	75	78	75
25645	80	68	60	54	65	63	58	58	68	57	65	62	63	63	67	58	70	89	79	70	61	75</												